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Proceedings

Pathological Society of Philadelphia

PROCEEDINGS

OF THE

PATHOLOGICAL SOCIETY

OF PHILADELPHIA.

NEW SERIES, VOLUME V.
OLD SERIES, VOLUME XXIII.

CONTAINING THE TRANSACTIONS OF THE SOCIETY FROM NOVEMBER, 1901, TO OCTOBER, 1902.

EDITED BY

DAVID RIESMAN, M.D.,

RECORDER OF THE SOCIETY.

PHILADELPHIA:
PRINTED FOR THE SOCIETY BY WM. J. DORNAN.
1902.

BOSTON MEDICAL
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RENÉ LA ROCHE, M.D., elected 1858.

ALFRED STILLÉ, M.D., LL.D., elected 1859, '61, and '62.

EDWARD HARTSHORNE, M.D., elected 1860 and '63.

J. M. DA COSTA, M.D., LL.D., elected 1864, '65, and '66.

JOHN H. PACKARD, M.D., elected 1867 and '68.

S. WEIR MITCHELL, M.D., LL.D., elected 1869.

JOHN ASHHURST, Jr., M.D., LL.D., elected 1870.

JAMES H. HUTCHINSON, M.D., elected 1871 and '72.

WILLIAM PEPPER, M.D., LL.D., elected 1873.

H. LENOX HODGE, M.D., elected 1876.

S. W. GROSS, M.D., elected 1879.

JAMES TYSON, M.D., elected 1882 and '83.

E. O. SHAKESPEARE, M.D., elected 1884.

J. C. WILSON, M.D., elected 1885 and '86.

F. P. HENRY, M.D., elected 1887 and '88.

HENRY F. FORMAD, M.D., elected 1889 and '90.

ARTHUR V. MEIGS, M.D., elected 1891 and '92.

J. H. MUSSER, M.D., elected 1893, '94, '95, and '96.

W. E. HUGHES, M.D., elected 1897 and '98.

F. A. PACKARD, M.D., elected 1899 and 1900.

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FEB 27 1903
E. H. B.

OFFICERS AND COMMITTEES

OF THE

PATHOLOGICAL SOCIETY OF PHILADELPHIA.

(Elected at the annual meeting, October 10, 1901.)

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SIMON FLEXNER, M.D.
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Business Committee.

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C. Y. WHITE, M.D.

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DAVID L. EDSALL, M.D.,
JOSEPH SAILER, M.D.

LIST OF MEMBERS.

ORIGINAL MEMBERS.

JOHN H. BRINTON, 1423 Spruce Street.
JAMES DARRACH, 5923 Greene Street, Germantown.
S. WEIR MITCHELL, 1524 Walnut Street.
GEORGE R. MOREHOUSE, 2033 Walnut Street.
THOMAS G. MORTON, 1617 Chessnut Street.
JOHN H. PACKARD, Hotel Stenton.

MEMBERS.

ELECTED
1894 Abbott, A. C., 4229 Baltimore Avenue.
1899 Adler, L. H., Jr., 1610 Arch Street.
1898 Allen, W. L., 3100 Wharton Street.
1889 Anders, J. M., 1603 Walnut Street.
1901 Anspach, B. M., 4824 Baltimore Avenue.
1900 Artelt, H., 1521 North Eighth Street.
1891 Ashton, Thomas G., 1814 South Rittenhouse Square.
1895 Ashton, William E., 2011 Walnut Street.
1902 Atlee, J. L., 206 East King St., Lancaster, Pennsylvania.

1897 Babcock, W. Wayne, 3302 North Broad Street.
1898 Baggs, Albert N., Abington, Pa.
1887 Baker, G. F., 1818 Spruce Street.
1888 Balliet, Tilghman M., 3705 Powelton Avenue.
1898 Bardsley, G., 2111 North Howard Street.
1885 Beates, Henry, Jr., 1504 Walnut Street.
1900 Behrend, Moses, 1331 North Franklin Street.
1871 Bennett, Wm. H., 2105 Spruce Street.
1887 Berens, Bernard, 2002 Chestnut Street.
1900 Bergey, D. H., 516 North Thirty-third Street.
1894 Beyea, H. D., 237 South Thirteenth Street.
1901 Biggs, M. H., 412 S. Fifteenth Street.
1892 Birney, D. B., 1810 De Lancey Place.
1898 Blackburn, A. E., Thirty-eighth and Spring Garden Streets.
1893 Bochroch, Max H., 987 North Eighth Street.

ELECTED
1886 Bodamer, George A., 1507 Girard Avenue.
1892 Boger, John A., 2213 North Broad Street.
1898 Boston, L. Napoleon, 1531 South Broad Street.
1893 Boyer, H. P., 1338 Spruce Street.
1898 Brinton, Ward, 1423 Spruce Street.
1896 Brown, H. MacV., 915 South Forty-ninth Street.
1895 Brubaker, A. P., 105 North Thirty-fourth Street.
1893 Bryan, J. Roberts, 4200 Chestnut Street.
1901 Buckley, A. C., 1705 North Fifteenth Street.
1887 Burr, Charles W., 1327 Spruce Street.

1902 Carncross, H. L., 1634 Pine Street.
1893 Carpenter, H. B., 1523 Locust Street.
1902 Carpenter, H. C., 1523 Locust Street.
1897 Carpenter, J. T., Jr., 1419 Walnut Street.
1900 Catanach, N. G., West Chester.
1887 Cattell, H. W., 3709 Spruce Street.
1898 Chestnut, J. E., 1817 Frankford Avenue.
1887 Chrystie, Walter, Bryn Mawr, Pennsylvania.
1899 Clark, John G., 218 South Fifteenth Street.
1866 Cleemann, Richard A., 2135 Spruce Street.
1898 Coates, George M., 2115 Locust Street.
1901 Coca, A. F., 122 South Thirty-third Street.
1900 Codman, C. A. E., 328 South Forty-second Street.
1872 Cohen, J. Solis, 1824 Chestnut Street.
1883 Cohen, S. Solis, 1525 Walnut Street.
1902 Cohen, W. Solis, 1313 Pine Street.
1896 Coley, Thomas Luther, 1219 North Sixth Street.
1890 Coplin, W. M. L., 1419 South Broad Street.
1901 Craig, F. A., 3417 Baring Street.
1899 Cruice, John M., 114 North Eighteenth Street.
1901 Cryer, M. H., 1420 Chestnut Street.
1898 Currie, Thos. R., 113 East Cumberland Street.
1871 Curtin, Roland G., 22 South Eighteenth Street.

1894 Da Costa, J. Chalmers, 1629 Locust Street.
1896 Da Costa, J. C., Jr., The Pascoe.
1885 Daland, Judson, 317 South Eighteenth Street.
1902 Dare, A. E., 2247 North Broad Street.
1900 Darrah, P. W., 3439 Woodland Avenue.

ELECTED
1890 Davis, C. N., 1931 Spruce Street.
1882 Davis, G. G., 255 South Sixteenth Street.
1893 Davisson, Alexander H., 2024 Pine Street.
1900 Deal, J. C., 5301 Haverford Avenue.
1889 Deaver, H. C., 1534 North Fifteenth Street.
1885 Deaver, J. B., 1634 Walnut Street.
1882 Dercum, F. X., 1719 Walnut Street.
1902 Dorrance, G. M., University Hospital.
1901 Dorsett, R. S., 1105 North Fortieth Street.
1894 Dougherty, S. W., 215 South Seventeenth Street.
1889 Downs, Norton, 102 West Walnut Lane, Germantown.
1877 Drysdale, T. M., 1305 Locust Street.
1866 Duer, Edward L., 1606 Locust Street.
1876 Dulles, C. W., 4101 Walnut Street.
1883 Dunmire, G. B., 1618 Spruce Street.
1860 Dunton, W. R., High Street and Germantown Avenue, Germantown.
1900 Dye, F. H., German Hospital.

1900 Eaton, W. B., Jefferson Medical College.
1896 Edsall, David L., 346 South Sixteenth Street.
1900 Elmer, W. G., 3904 Locust Street.
1900 Erck, T. A., 338 South Sixteenth Street.
1891 Eshner, A. A., 224 South Sixteenth Street.

1901 Farr, C. B., 4603 Cedar Avenue.
1892 Fenn, William B., Denver, Col.
1881 Fenton, T. H., 1319 Spruce Street.
1876 Fisher, Henry M., 317 South Twelfth Street.
1899 Flexner, S., Medical Department, University of Pennsylvania.
1894 Fox, L. Webster, 1304 Walnut Street.
1899 Francine, A. P., 1404 Spruce Street.
1895 Frazier, Charles Harrison, 133 South Eighteenth Street.
1894 French, Samuel, Plymouth, Pa.
1889 Frese, Carl, German Hospital.
1890 Friebis, George, 1906 Chestnut Street.
1885 Fussell, M. H., 189 Green Lane, Manayunk.

1895 Garitee, C. J., 1117 Spruce Street.
1901 Gay, F. P., 217 South Fifteenth Street.
1902 Geisler, Howard D., 202 High Street, Germantown.

ELECTED
1897 Gerson, T. P., Lansdowne.
1870 Getchell, Frank H., 1432 Spruce Street.
1902 Gildersleeve, Nathaniel, Laboratory of Hygiene, Univ. of Penna.
1902 Gilliland, S. H., University Dormitories.
1900 Gilpin, S. F., Fifty-fifth and Girard Avenue.
1894 Girvin, John H., 3912 Walnut Street.
1902 Githens, T. S., 835 South Forty-ninth Street.
1898 Gittings, J. Claxton, 4013 Chestnut Street.
1899 Given, E. E. W., 2714 Columbia Avenue.
1882 Godey, H. E., N. E. corner Nineteenth and Spruce Streets.
1900 Goepp, R. M., 1713 Pine Street.
1902 Graham, C. E., 1713 Spruce Street,
1890 Grayson, C. P., 251 South Sixteenth Street.
1867 Grier, Matthew J., 1531 Spruce Street.
1883 Griffith, J. P. C., 123 South Eighteenth Street.
1897 Gross, Wm., 701 North Fortieth Street.
1890 Gummey, Frank B., 5418 Greene Street, Germantown.
1900 Gwyn, N. B., 225 South Twentieth Street.

1893 Hamill, S. M., 1822 Spruce Street.
1893 Hand, Alfred, Jr., 1724 Pine Street.
1885 Hare, Hobart Amory, N. W. cor. Eighteenth and Spruce Streets.
1902 Harland, W. G., 126 South Nineteenth Street.
1898 Hart, Chas. D., Pennsylvania Hospital.
1890 Hartzell, M. B., 3634 Chestnut Street.
1901 Hawke, W. W., Philadelphia Hospital.
1900 Head, J., 1431 Walnut Street.
1873 Hearn, W. Joseph, 1120 Walnut Street.
1870 Henry, Frederick P., 1635 Locust Street.
1896 Henry, John N., 1635 Locust Street.
1880 Hewson, Addinell, Jr., 1508 Pine Street.
1901 Hickman, W. A., 324 South Sixteenth Street.
1899 Hitchens, A. P., Glenolden, Pennsylvania.
1902 Hodge, E. D., 346 South Fifteenth Street.
1899 Holloway, T. B., 5505 Haverford Avenue.
1894 Hughes, George M., 241 North Eighteenth Street.
1882 Hughes, W. E., 3945 Chestnut Street.
1901 Hunsicker, C. H., German Hospital.
1902 Hunter, John W., University Hospital.

1901 Irwin, J. W., 1918 Vine Street.

ELECTED
1890 Jarrett, Henry, Camden, N. J.
1895 Jopson, J. H., 334 South Sixteenth Street.
1898 Judson, Chas. F., 2010 De Lancey Street.
1899 Jump, H. D., 4634 Chester Avenue.
1885 Jurist, L., 916 North Broad Street.

1898 Kalteyer, F. J., 214 South Sixteenth Street.
1901 Kane, J. A. B., 258 South Fifteenth Street.
1895 Kelly, A. O. J., 1911 Pine Street.
1899 Kennedy, L. F., Marcus Hook, Pa.
1890 Ketcham, S. Rush, 1708 Green Street.
1897 King, W. H., 412 South Fifteenth Street.
1902 Kinyoun, J. J., Glenolden, Pennsylvania.
1888 Kirby, Ellwood R., 1202 Spruce Street.
1900 Kirk, E. C., Dental Hall, University of Pennsylvania.
1900 Klapp, W. P., 1716 Spruce Street.
1897 Klein, Alexander, 721 Spruce Street.
1890 Kneass, Samuel S., 1510 Walnut Street.
1898 Knipe, J. C., S. E. corner Fifteenth and Diamond Streets.
1901 Kohn, B., 1523 North Eighth Street.
1895 Krusen, Wilmer, 158 North Twentieth Street.
1892 Kyle, D. Braden, 1517 Walnut Street.

1899 Landis, H. R. M., 225 South Twentieth Street.
1890 Laplace, Ernest, 1828 South Rittenhouse Square.
1898 Latta, Samuel W., 3626 Baring Street.
1894 Leach, W. W., 2118 Spruce Street.
1869 Leaman, Henry, 828 North Broad Street.
1888 Leidy, Joseph, 1319 Locust Street.
1887 Leopold, Isaac, 1520 Franklin Street.
1902 Levi, J. V., 1733 North Sixteenth St.
1875 Lewis, Morris J., 1316 Locust Street.
1894 Lincoln, C. W., Ridley Park, Pennsylvania.
1899 Lindauer, Eugene, 1917 North Thirty-second Street.
1886 Lloyd, James Hendrie, 3910 Walnut Street.
1898 Lodholtz, Edward, 3103 Diamond Street.
1894 Loeb, Ludwig, 1421 North Fifteenth Street.
1902 Loeb, V. A., 957 North Eighth Street.
1875 Longstreth, Morris, 1416 Spruce Street.
1902 Luther, J. W., 415 South Fifteenth Street.

ELECTED
1896 McCarthy, D. J., 1342 Pine Street.
1880 McClellan, George, 1352 Spruce Street.
1901 McConnell, G., 112 South Eighteenth Street.
1892 McFarland, J., 421 West Price Street, Germantown.
1894 McKee, James H., 1519 Poplar Street.
1890 McKelway, George I., 114 South Eighteenth Street.
1902 McKenna, J. A., Lansdowne, Pennsylvania.
1894 McLeod, George, Ardmore.
1898 McReynolds, R. P., 3722 Walnut Street.
1899 Masland, M. C., 2134 North Nineteenth Street.
1892 Massey, Frank, 3604 Locust Street.
1864 Mears, J. Ewing, 1429 Walnut Street.
1873 Meigs, Arthur V., 1322 Walnut Street.
1878 Mills, C. K., 1909 Chestnut Street.
1901 Mitchell, C. F., Pennsylvania Hospital.
1884 Mitchell, J. K., 256 South Fifteenth Street.
1896 Modell, D. A., 242 Fairmount Avenue.
1900 Moore, E. K., 1715 Walnut Street.
1898 Morris, Henry, 315 South Sixteenth Street.
1885 Morrison, William H., Holmesburg, Pennsylvania.
1887 Morton, S. W., 113 South Twentieth Street.
1869 Müller, August F., 5429 Greene Street, Germantown.
1899 Müller, G. P., German Hospital.
1880 Musser, J. H., 1927 Chestnut Street.
1898 Myers, A. W., Episcopal Hospital.

1879 Neff, J. S., S. W. corner Twenty-third and Spruce Streets.
1900 Newlin, A., Pennsylvania Hospital.
1898 Newton, R. D., 1504 Arch Street.
1902 Noble, C. P., 1509 Locust Street.
1901 Norris, C. C., 1503 Locust Street.
1900 Norris, G. W., 1530 Locust Street.

1894 O'Malley, James, 1104 Jackson Street.
1900 O'Reilly, C., N. E. corner Fifty-third and Haverford Avenue.
1898 Ostheimer, A. J., Jr., 1229 Locust Street.
1897 Ostheimer, Maurice, 225 South Twentieth Street.

1885 Packard, F. A., 258 South Eighteenth Street.
1893 Packard, F. R., 1831 Chestnut Street.
1900 Pancoast, H. K., 118 South Thirty-fourth Street.

ELECTED

1901 Patterson, F. D., 1503 Locust Street.
1901 Paul, F. M., German Hospital.
1892 Pearce, F. S., 1407 Locust Street.
1900 Pearce, R. M., Medical Department, University of Pennsylvania.
1900 Pearson, L., Veterinary Department, University of Pennsylvania.
1897 Pepper, William, 1811 Spruce Street.
1895 Perkins, F. M., 1428 Pine Street.
1897 Peters, L. C., 2136 Oxford Street.
1902 Pfahler, G. E., Philadelphia Hospital.
1901 Pickett, W., 1508 North Fourth Street.
1885 Piersol, G. A., 4722 Chester Avenue.
1890 Potts, C. S., 1726 Chestnut Street.
1900 Prince, D. H., Jefferson Medical College.
1901 Purves, G. M., 750 South Tenth Street.

1901 Ranck, E. M., Glenolden, Pennsylvania.
1902 Randolph, B. M., Polyclinic Hospital.
1885 Randall, B. A., 1717 Locust Street.
1898 Ravenel, M. P., University of Pennsylvania, Veterinary Department.
1894 Reckefus, C. H., 506 North Sixth Street.
1885 Reed, Boardman, 1831 Chestnut Street.
1899 Reynolds, W., 1322 Pacific Avenue, Atlantic City.
1894 Rhein, J. H. W., 334 South Fifteenth Street.
1894 Riesman, David, 326 South Sixteenth Street.
1891 Ring, G. O., S. W. corner Nineteenth and Chestnut Streets.
1876 Roberts, John B., 1627 Walnut Street.
1884 Robertson, W. E., 912 North Fourth Street.
1902 Robins, Albert, Newark, Delaware.
1901 Robinson, E. T., 1326 Pine Street.
1889 Robinson, William Duffield, 2012 Mount Vernon Street.
1899 Rodman, W. L., 1626 Spruce Street.
1898 Rosenberger, R. C., 2330 North Thirteenth Street.
1891 Rosenthal, E., 517 Pine Street.
1894 Ross, George, 219 South Seventeenth Street.
1900 Roussel, A. E., 2112 Pine Street.
1900 Roxby, J. B., 2222 North Nineteenth Street.

1896 Sailer, Joseph, 248 South Twenty-first Street.
1867 Santee, Eugene J., 532 North Sixth Street.
1890 Sartain, Paul J., 212 West Logan Square.

ELECTED
1895 Schamberg, J. F., 1636 Walnut Street.
1901 Schamberg, M., 1636 Walnut Street.
1882 de Schweinitz, G. E., 1401 Locust Street.
1890 Scott, J. A., 1834 Pine Street.
1898 Sharpless, Wm. T., West Chester, Pa.
1902 Shields, W. G., Jr., 412 West School House Lane, Germantown.
1885 Shober, J. B., 1731 Pine Street.
1889 Shoemaker, Harvey, 109 South Twentieth Street.
1895 Shumway, E. A., 2007 Chestnut Street.
1899 Sinclair, J. F., 200 South Fortieth Street.
1868 Sinkler, Wharton, 1606 Walnut Street.
1901 Siter, E. D., 2038 Locust Street.
1881 Skillern, P. G., 241 South Thirteenth Street.
1898 Smyth, Henry Field, Germantown Hospital.
1902 Somers, L. A., 3554 North Broad Street.
1894 Spellissy, Joseph M., 110 South Eighteenth Street.
1896 Spiller, William G., 4409 Pine Street.
1890 Stahl, B. F., 1502 Arch Street.
1901 Stanton, W. B., 412 South Fifteenth Street.
1894 Steele, J. D., Fortieth and Locust Streets.
1889 Stengel, Alfred, 1811 Spruce Street.
1900 Stetson, J. B., 1336 Spruce Street.
1889 Stevens, Arthur A., 314 South Sixteenth Street.
1896 Stewart, Alonzo H., 250 North Twelfth Street.
1886 Stewart, David D., 1429 Walnut Street.
1902 Stiles, F. A., 3300 Spring Garden Street.
1899 Stout, G. C., 1726 Chestnut Street.
1884 Stritmatter, I. P., 999 North Sixth Street.
1869 Stryker, Samuel S., 3833 Walnut Street.
1894 Swan, John M., 3713 Walnut Street.
1902 Sweet, J. E., University Dormitories.

1899 Taggart, T. D., 1825 Fairmount Avenue.
1900 Talley, J. E., Fifty-sixth and Lansdowne Avenue.
1897 Teller, Wm. H., 1934 Green Street.
1894 Thomas, W. Hersey, 1445 North Seventeenth Street.
1894 Thomson, Archibald G., 1426 Walnut Street.
1868 Thomson, William, 1426 Walnut Street.
1902 Thornton, E. Q., 922 Spruce Street.
1899 Tinker, M. B., 1533 Pine Street.

ELECTED
1902 Tracy, S. E., 1337 Spruce Street.
1897 Tucker, Henry, 19 South Twenty-first Street.
1898 Twaddell, Thomas, 4203 Chester Avenue.
1863 Tyson, James, 1506 Spruce Street.
1890 Tyson, T. Mellor, 1506 Spruce Street.

1900 Uhle, A. A., 1439 North Fifteenth St.

1895 Vandervoort, C. A., 3250 North Fifteenth Street.
1887 Vansant, Eugene L., 1929 Chestnut Street.

1898 Wadsworth, W. S., 227 South Thirty-sixth Street.
1891 Wallace, James, 350 South Sixteenth Street.
1899 Walsh, J. P., 732 Pine Street.
1890 Warder, C. B., 1401 North Sixteenth Street.
1874 Warder, W. H., 1212 North Broad Street.
1895 Wendell, W. G., 4126 Chester Avenue.
1887 Westcott, T. S., 1833 Spruce Street.
1902 Wetherill, H. E., 3734 Walnut Street.
1885 Wharton, H. R., 1725 Spruce Street.
1897 White, Courtland Y., 334 South Sixteenth Street.
1873 White, J. William, 1810 South Rittenhouse Square.
1893 Whiting, A. D., 1523 Spruce Street.
1868 Willard, De Forest, 1818 Chestnut Street.
1898 Willson, R. N., 350 South Fifteenth Street.
1869 Wilson, James C., 1437 Walnut Street.
1891 Wilson, Samuel M., 1517 Arch Street.
1891 Wilson, W. R., 112 South Twentieth Street.
1895 Witmer, A. F., 1328 Pine Street.
1900 Wister, J. W., 5277 Germantown Avenue.
1890 Wood, A. C., 128 South Seventeenth Street.
1898 Wood, George B., 129 South Eighteenth Street.
1865 Woods, D. Flavel, 1501 Spruce Street.
1897 Woodward, E. B., 4222 Chestnut Street.
1898 Woodward, G., Chestnut Hill.
1899 Worden, C. B., 4208 Walnut Street.

1897 Yarrow, Thomas J., Jr., 1739 North Sixteenth Street.

1895 Zimmerman, Mason W., 1522 Locust Street.
1902 Zuirleck, A. J., 6236 Woodland Avenue.

NON-RESIDENT MEMBERS.

Baines, A. S., Jr., 4484 Finney Avenue, St. Louis, Mo.
Ball, M. V., Warren, Pa.
Breinig, P. B., Bethlehem, Pa.
Carter, W. S., Galveston, Texas.
Cerna, D., Galveston, Texas.
Dock, George, Ann Arbor, Mich.
Edwards, W. A., San Diego, Cal.
Egbert, Joseph P., Wayne, Delaware County, Pa.
Eskridge, J. T., Denver, Col.
Fox, J. M., Torresdale, Pa.
Gaylord, H. R., Buffalo, N. Y.
Hamaker, W. D., Meadville, Pa.
Hamann, C. A., 517 Euclid Avenue, Cleveland, Ohio.
Harris, H. F., Atlanta, Georgia.
Harrison, W. H., Harrisburg, Pa.
Hatch, John L., 2010 Fifth Avenue, New York City.
Hileman, J. B., Altoona, Pa.
Hiller, H. H.
Holder, C. A., Colorado Springs, Col.
Howard, F. H., Williamstown, Massachusetts.
Hunt, J. R., New York.
Izard, W., Camden, New Jersey.
Jamar, John H., Elkton, Md.
Johnston, J. A., National Soldiers' Home, Virginia.
Lincoln, W. R., Cleveland, O.
Muhlenberg, Frank, Reading, Pa.
Nancrede, C. B., Ann Arbor, Mich.
Osler, William, Johns Hopkins Hospital, Baltimore, Md.
Pease, H. D., Buffalo, N. Y.
Pfouts, G. B., Morris Plains, N. J.
Powell, W. M., Atlantic City, N. J.
Rahter, C. A., Harrisburg, Pa.

Rivas, Damoso, Lille, France.
Schreiner, E. R., U. S. A.
Slifer, Henry F., North Wales, Pa.
Smith, Allen J., Galveston, Texas.
Stadelman, E., Durango, Mexico.
Stiles, G. A., Conshohocken, Pa.
Stubbs, R. P., Wilmington, Delaware.
Taylor, A. E., University of California, San Francisco, California.
Taylor, L. H., Wilkesbarre, Pa.
Toulmin, H., Haverford, Pa.
Wells, G. M., Wayne, Delaware County, Pa.
Wetherill, R. B., Lafayette, Ind.
White, Frank, Elwyn.
Williams, H. L., Minneapolis, Minnesota.
Wilmarth, A. W., State Home for the Feeble Minded, Chippewa Falls, Wisconsin.
Ziegler, J. L., Mt. Joy, Pennsylvania.

CORRESPONDING MEMBERS.

ELECTED	
1866	Bumstead, Freeman J. Deceased.
1859	Clark, Alonzo, New York. Deceased.
1898	Cornil, V., Faculté de Médecine, Paris, France.
1859	Dalton, J. C., New York. Deceased.
1885	Dent, Clinton T., Assistant Surgeon and Lecturer on Practical Surgery at St. George's Hospital, Surgeon to Belgrave Hospital for Children, London, England.
1860	Ellis, Calvin. Deceased.
1888	Fedeli, Gregorio, Rome, Italy.
1858	Flint, Austin, Sr. Deceased.
1890	Gibbes, Heneage, Ann Arbor, Michigan.
1858	Hammond, William A., New York. Deceased.
1860	Isaacs, Charles E., Brooklyn. Deceased.
1878	Jackson, J. B. S., Boston. Deceased.
1886	Pye-Smith, P. H., Physician and Lecturer on Medicine at Guy's Hospital, London, England.
1860	Reeves, James E., Wheeling, West Virginia. Deceased.
1861	Rokitansky, Carl. Deceased.
1898	Virchow, Rudolf, Berlin, Germany. Deceased.
1860	Watson, John, New York. Deceased.
1898	Welch, William H., Professor of Pathology, Johns Hopkins University, Baltimore, Maryland.
1859	Worthington, Wilmer, West Chester, Pennsylvania. Deceasad.

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The Identification of the Colon Bacillus by Reactions Produced in Culture Media Containing Neutral Red. Observations on Reactions of Other Bacteria on the Same Media.

R. C. ROSENBERGER, M.D.

(*From the Laboratories of the Jefferson Medical College Hospital.*)

It has been stated by several authorities that neutral red agar is a good medium for differentiating the Bacillus coli communis from the Bacillus typhosus. Furthermore, it has been claimed by Rothberger and Hunter that the Bacillus coli communis upon this medium produces a fluorescence, and that the medium is turned to a yellowish color—nearly a canary yellow.

(Neutral red—neutralroth—according to Lee,[1] is a basic color. The term "neutral" refers to the hue of its solution and not to its chemical composition. Its neutral red tint is turned bright red by acids, and yellow by alkalies.)

From the above apparently specific reaction Hunter[2] claims that he has been able to detect the presence of the colon bacillus in water supplies by simply inoculating the water upon this medium and obtaining the above reaction. If the test can be relied upon, one can readily see the importance of such a medium for the detection and identification of an organism so closely resembling the Bacillus typhosus. As the reaction of the colon bacillus was alleged to be characteristic, the writer undertook experiments with other organisms with the object of determining if the colored media yielded any other important differentiating test.

Savage[3] uses a 0.5 per cent. glucose neutral red bouillon for the routine examination of water where the Bacillus coli is suspected. His method is to add 10 c.c. of water to a tube of ½ per cent. glucose neutral red bouillon, then to 40 c.c. of water add the contents of a second tube of neutral red bouillon. Incubate at 37° C. and examine daily up to seventy-two hours. Of fifty waters examined he obtained thirty-nine positive results—that is, fluorescence and the red color reduced to yellow or orange.

Of thirty-four waters especially examined for the Bacillus coli communis a positive result occurred in thirty-one, and the organism was isolated therefrom in thirty-one samples.

Pakes[4] claims that the same reaction takes place with the Bacillus proteus vulgaris, Bacillus prodigiosus, Bacillus killiense, Bacillus lactis aerogenes, and all the members of the enteritis groups of Gaërtner and Friedländer.

Hunter claims that the Bacillus œdematis maligni, Bacillus proteus vulgaris, Bacillus prodigiosus, Bacillus tetani also give the same reaction. He draws the following conclusions:

1. That the Bacillus coli communis and a few other micro-organisms possess the power of reducing neutral red to a canary yellow fluorescent color.

2. That the Bacillus typhosus never possesses this power of reduction.

3. That it is possible within twelve to twenty-four hours to diagnose with accuracy by means of neutral red the typhoid group of micro-organisms from the true colon group.

In the experiments detailed below the medium was made by using ordinary peptone agar and adding five drops of a saturated watery solution of the dye to each tube containing 15 c.c. of neutral agar. No definite formula for preparing the medium has been published. The medium was then sterilized and allowed to "set" as ordinary slant agar. Inoculations were made upon the medium, and the reaction was noticed in the tubes from twenty-four hours to five days. The cultures and controls, with the exception of the bacillus of tetanus, were incubated at 37° C.

The cultures of the Bacillus coli communis were as nearly typical as could be desired, and as everyone knows that all reactions or characters of a certain bacterium are not constantly obtainable, so one or two characters of this bacterium failed to develop.

In the cultures (*a*) to (*g*) the bacilli were all motile; their growth on agar was of a grayish-white color; they all possessed an acid reaction, turning blue litmus milk red, and in cultures (*a*), (*b*), (*c*), (*d*), (*e*), and (*f*) producing firm coagula; in culture (*g*) no coagula were observed.

In bouillon they all clouded the medium, and in cultures (*a*), (*c*), (*e*), and (*f*) a delicate pellicle was observed.

Upon potato the growth of all the cultures was of a yellowish-brown color. Gas developed in cultures (*c*), (*d*), and (*e*); no gas was demonstrable in the other cultures. Indol was produced in cultures (*b*), (*c*), (*d*), (*e*), and (*f*), but was absent in cultures (*a*), and (*g*).

In series (1), (2), and (3) the bacilli were motile; the growth upon agar was of a grayish-white color, and all possessed iridescence. They all possessed slight acid properties, evidenced by rendering blue litmus milk pink; coagulation was observed only in tube (1). In bouillon they all clouded the medium and formed a delicate pellicle upon the surface of the medium. Upon potato the growth was of a brownish color. Abundant gas production was present in culture (1); none was present in the other two tubes. Indol was produced in all three cultures.

The bacillus obtained from Dr. Wayne Babcock was motile; the growth upon agar was at first grayish-white in color, and later light brown. It coagulated milk. In bouillon it clouded the medium, without formation of a pellicle. Upon potato the growth was of a brownish color. Gas formation and indol production were present.

In two cultures of the writer's the growth upon agar was of a grayish-white color, milk was coagulated, bouillon was clouded, and a pellicle formed on the surface of the medium. Upon potato the growth was brownish in color. Gas formation was present in both cultures. Indol production was present in one and absent in the other. All the bacilli used were negative to Widal's reaction.

Seven cultures of the Bacillus coli communis were obtained from Dr. N. Gildersleeve, and lettered from (*a*) to (*g*). These were inoculated upon the neutral red medium, and gave the following results:

Bacillus coli communis (*a*): The growth is of a pinkish color, with fading of the color, and a deposit of small red crystals throughout the medium.

Bacillus coli communis (*b*): The growth is of a dark red color, with fading of the color and the deposit of small red crystals throughout the medium.

Bacillus coli communis (*c*): The growth is of a dark yellowish-brown color, with slight fading of the color of the medium, and the deposit of small red crystals throughout.

Bacillus coli communis (*d*): The growth is of a light pinkish color, with slight fading of the color of and the deposit of small red crystals throughout the medium.

Bacillus coli communis (*e*): The growth is of a very light pinkish-red color, with fading of the color of the medium and the deposit of small red crystals throughout.

Bacillus coli communis (*f*): The growth is of a pinkish color, with fading of the color of and the deposit of small red crystals throughout the medium.

Bacillus coli communis (*g*): The growth is of a light gray color, with no appreciable fading of the color of the medium.

Another culture obtained from Dr. Babcock was tried upon the medium. The growth was of a reddish color, and a slight fluorescence developed; there was no fading of the color of the medium. Iridescence was noticed upon ordinary agar.

Three cultures (1), (2), and (3) of the colon bacillus obtained from Dr. Gilliland (Laboratory of Veterinary Medicine, University of Pennsylvania) were also inoculated into neutral red agar.

Bacillus (1). The growth is of a dark-red color, with fading of the color of the medium and the deposit of small red crystals throughout.

Bacillus (2): The growth is pinkish in color, with slight fading of the color of the medium and the deposit of small red crystals throughout; later the medium turned to a brownish color; no fluorescence was demonstrable.

Bacillus (3): The growth is reddish in color, with marked fading of the color of the medium and the deposit of small reddish crystals throughout.

Iridescence was observed in all three cultures upon glycerin agar. In the series of cultures obtained from Dr. Gildersleeve (*b*) and (*c*), after fourteen days the growth turned to a yellowish-brown color, but no fluorescence was demonstrable.

A second series of experiments was carried out with the Bacillus coli communis and the other organisms named by melting agar and adding five drops of a saturated watery solution of neutral red, resterilizing, and when sufficiently cool inoculating and incubating at 37° C.

These tubes were not slanted. Plates were also made of the Bacillus coli communis and Bacillus typhosus with neutral red agar, but there was no essential difference in the behavior of the growths. Each was attended by complete decolorization of the medium, as Hunter has observed; hence, there is no differentiating point in plate cultures between the two organisms in question.

In the one series of cultures lettered (*a*) to (*g*) inclusive the following reactions were noticed after twenty-four hours:

Culture (*c*) presented a more or less brownish color, with slight fluorescence. It resembles the reaction observed when powdered eosin is dropped in water.

Culture (*d*) presented a dark brown color of the medium, especially at the bottom of the tube; no fluorescence was demonstrable.

In the other cultures (*a*), (*b*), (*e*), (*f*), and (*g*) no reaction was demonstrable; neither changing of the color of the medium nor fluorescence was seen.

In the series numbered (1) to (3) inclusive the color of the medium of (2) has faded; no further reaction was observed.

In (3) a brownish color took the place of the dark red, and there was a slight fluorescence observed.

In (1) no reaction was demonstrable.

In still another culture no reaction was observed.

In a culture that was obtained from the feces a greenish-yellow color of the medium was observed at the bottom of the tube, which also possessed the fluorescence mentioned above, but more marked.

In seventy-two hours the following observations were made:

Culture (*c*) mentioned above presents quite a marked fluorescence, while the color of the medium was more or less reddish-yellow.

Culture (*f*), while not showing any change in the color of the medium, shows fluorescence upon the surface.

Culture (*d*) shows very slight fluorescence, together with the dark brown color of the medium above mentioned.

In the other cultures (*a*), (*b*), (*e*), and (*g*) no reaction was demonstrable.

In seventy-two hours, in the series (1), (2), and (3), (2) shows a slight fluorescence upon the surface of the medium; (3) shows a marked fluorescence upon the surface and slight fluorescence throughout the medium.

There is no reaction seen in (1).

In Dr. Babcock's specimen no reaction was demonstrable; in the culture obtained from the feces no reaction was obtained—neither fluorescence nor turning of the color of the medium from a red to a yellow color after seventy-two hours' observation.

It will be seen from the latter experiments that thirteen different cultures of the Bacillus coli communis were used.

The reactions were noticed after twenty-four hours and up to five days. In but seven of the cultures was fluorescence demonstrable, while not one of the cultures showed the canary-yellow color described by Rothberger and Hunter. In only one case was marked fluorescence seen.

In four cultures the fluorescence was demonstrable in twenty-four hours, while in the other three this reaction was not observed until seventy-two hours had elapsed. The reaction is said to take place in twenty-four hours, and while some did react in this time many of the cultures did not. Even after five days' observation no other changes occurred.

Why this reaction (fluorescence) should take place in the latter experiments, and not in the experiments undertaken with slant tubes of agar, is hard to explain. It may be accounted for by the partly anaerobic atmosphere in which the organism is compelled to grow. Supposing this to be the case, the writer then placed the cultures in a Novy jar and subjected them to an atmosphere of hydrogen for forty-eight hours. No further reaction occurred.

In the experiments with the other organisms the reaction was similar to that obtained in ordinary slant tubes. No fluorescence was demonstrable in any of the tubes.

A third series of experiments was conducted with 0.5 per cent. glucose neutral red bouillon, with thirteen different cultures of the Bacillus coli communis and the other organisms named below. The inoculated tubes were placed in the incubator at 37° C. and observed daily for five days. In only one tube of Bacillus coli communis was fluorescence observed. This reaction and yellow color described were quite marked.

Not one of the other cultures of Bacillus coli communis nor the other organisms mentioned gave the fluorescence or the reduction of the red color to yellow or orange up to five days.

Fading of the color of the medium from red to pink was noticed in four cultures of Bacillus coli communis, and two cultures each of Bacillus typhosus, Bacillus prodigiosus, and Vibrio Schuylkilliensis. After thirteen days had elapsed slight fluorescence was present in one culture of Bacillus prodigiosus and Bacillus fluorescens.

The following are experiments made upon the same media with other bacteria:

The growth of the Bacillus typhosus is of a very delicate pink color, with fading of the color of the medium.

Bacillus dysenteriæ (Flexner) grows as light-reddish colored colonies, attended by a slight fading of the color of the medium.

The growth of the Bacillus megatherium is of a dark red color, and attended by fading of the color of the medium.

The Bacillus putrificus coli also grows as dark red colonies, and the color of the medium fades slightly.

The Bacillus figurans grows as reddish colonies, with no appreciable fading of the color of the medium.

The colonies of the Bacillus capsulatus (Pfeiffer) are of a reddish color, with marked fading of the color of the medium.

The colonies of the Bacillus subtilis are reddish in color, and there is marked fading of the dye, with a deposit of small red crystals throughout the medium.

The growth of the Bacillus prodigiosus is of a dull pinkish color, with fading and the deposit of small red crystals throughout the medium.

Monilla conidia grows as reddish-colored colonies, with no perceptible fading of the color of the medium.

The growth of the bacillus of swine plague is of a pinkish color, with slight fading of the color of the medium and the deposit of small red crystals throughout.

The growth of the bacillus of tetanus is of a faint pink color; slight fading of the color of the medium occurs. (A sterile tube of neutral red agar was placed in an anaerobic condition; there was no fading of the color demonstrable up to ten days.)

The growth of Sarcina aurantiaca is of a reddish color, with slight fading of the color of the medium.

The growth of Sarcina lutea is of a dark-reddish color, with marked fading of the color of the medium.

Sanarelli's bacillus grows as light-reddish colored colonies, and shows very slight change in the color of the medium.

The growth of the Bacillus pyocyaneus is of a grayish-white color or slightly yellowish; the red color gradually faded from the medium, and there was no appearance of any greenish color.

The growth of the Bacillus anthracis is pink; the medium fades until it becomes colorless, in seventy-two hours.

The growth of the Bacillus mallei is also of a pinkish color; the color of the medium fades, especially where the growth is marked and piled up.

The growth of the Micrococcus roseus is of a deep pink color; the color of the medium fades, especially where the growth is most marked.

The growth of the Bacillus janthinus is entirely colorless, with fading of the color of the medium.

The growth of the Bacillus diphtheriæ is of a reddish tint, with fading of the color of the medium. The growth of the pseudodiphtheria bacillus presents no essential difference from the true diphtheria bacillus.

The growth of the Bacillus mesentericus vulgatus is deep pink, with fading of the color of the medium.

The growth of the Bacillus fluorescens liquefaciens (water) is of a deep pink color; the medium does not fade; a slight fluorescence appears.

The growth of Leptothrix epidermidis is pinkish, and the color of the medium fades.

The growth of a pink diplococcus (obtained from water) is of a deep red color, and the fading of the color of the medium is marked.

The growth of Bacillus Havaniensis (Sternberg) is deep red, and the color of the medium fades but slightly.

The growth of the bacillus of fowl enteritis is pinkish, and the color of the medium fades.

The growths of the Staphylococcus pyogenes albus and aureus were of pinkish color, and the color of the medium faded in each case.

The growth of the Bacillus hæmatoides is deep pink or almost reddish, while fading of the color of the medium is conspicuous.

The growth of the Vibrio Schuylkilliensis is of a light pinkish color, with slight fading of the color of the medium.

The growth of the spirillum of Asiatic cholera is of a light pinkish color, with marked fading of the color of the medium.

The growth of the Vibrio Metchnikovi is light yellow, and the medium fades slightly.

Table of Reactions of the Bacillus Coli Communis and other Organisms upon Neutral Red Agar and one-half per cent. Glucose Neutral Red Bouillon.

X Fluorescence. — No fluorescence. + Fading of color of the medium.

Organisms.	*Neutral Red Agar.*	*One-half per cent. Glucose Neutral Red Bouillon.*
Bacillus coli communis (*a*)	—	— +
Bacillus coli communis (*b*)	—	—
Bacillus coli communis (*c*)	X	— +
Bacillus coli communis (*d*)	X	— +
Bacillus coli communis (*e*)	—	—
Bacillus coli communis (*f*)	X	— +
Bacillus coli communis (*g*)	—	—
Bacillus coli communis (1)	—	—
Bacillus coli communis (2)	X	—
Bacillus coli communis (3)	X	—

*

Organisms.	*Neutral Red Agar.*	*One-half per cent. Glucose Neutral Red Bouillon.*
Bacillus coli communis (B)	X	X
Bacillus coli communis (X)	—	—
Bacillus coli communis (Y)	X	—
Bacillus anthracis	— +	—
Bacillus mallei	— +	—
Micrococcus roseus	— +	—
Bacillus janthinus	— +	—
Bacillus diphtheriæ	— +	—
Pseudodiphtheria bacillus	— +	—
Bacillus mesentericus vulgatus	— +	—
Bacillus fluorescens liquefaciens	X +	X +
Leptothrix epidermidis	— +	—
Diplococcus (pink)	— +	—
Bacillus Havaniensis (Sternberg)	— +	—
Bacillus of fowl enteritis	— +	—
Staphylococcus pyogenes aureus	— +	—
Staphylococcus pyogenes albus	— +	—
Bacillus hæmatoides	— +	—
Spirillum of Asiatic cholera	— +	—
Vibrio Metchnikovi	— +	—
Spirillum of Finkler and Prior	— +	—
Bacillus typhosus	— +	— +
Bacillus dysenteriæ (Flexner)	— +	—
Bacillus tetani	— +	—
Sarcina aurantiaca	— +	—
Sarcina lutea	— +	—
Sanarelli's bacillus	— +	—
Bacillus megatherium	— +	—
Bacillus putrificus coli	— +	—
Bacillus figurans	—	—
Bacillus capsulatus (Pfeiffer)	— +	—
Bacillus subtilis	— +	—
Bacillus prodigiosus	— +	X +
Bacillus of swine plague	— +	—
Bacillus pyocyaneus	— +	—
Proteus vulgaris	— +	—
Vibrio Schuylkilliensis	— +	—
Bacillus alcaligenes	—	X

The writer's conclusions are:

1. That, while not affording a specific reaction in the case of the Bacillus coli communis, neutral red agar should be classed as a valuable differentiating medium.

2. The typhoid bacillus, while it does cause a fading of the color of the medium, never gives rise to the fluorescence noticed in some cultures of the Bacillus coli communis.

3. Further, the test medium should not be depended upon as the only differentiating one in examination of water, as several very common bacteria found in the water give the same reaction.

The writer wishes to express his thanks to Drs. N. Gildersleeve, Gilliland, and Babcock for cultures of the Bacillus coli communis used in the experiments. The writer also wishes to thank Dr. Bergey for several cultures of other bacteria.

NOTE.—Since this paper was read the papers by Makgill and by Savage have appeared in the *Journal of Hygiene*, vol. i., No. 4, pp. 430 and 437. *October* 24, 1901.

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Amebic Abscess of Liver.

J. ALISON SCOTT, M.D.

The specimen presented was removed from Robert G., colored, aged forty years, by occupation a laborer, who was admitted to the Pennsylvania Hospital on July 17, 1901, under the care of Dr. Morris J. Lewis.

Abstract of History. Family history is negative, except his mother is said to have died of phthisis. Personal history: Had smallpox when a child; always subject to asthmatic attacks of short duration. In 1899, "a fever," in Charleston, S. C. Denies any intestinal disease, such as diarrhea or dysentery. Once acknowledged he had a bloody diarrhea, then subsequently denied it. Illness for which he was admitted began suddenly on July 14th, with sharp knife-like pains in the right side, with intense dyspnea. On admission he presented all the physical signs of massive effusion of right pleura, with great displacement of the heart and liver. The liver was palpable midway between xiphoid and umbilicus, firm and tender. Spleen not enlarged. Urine was albuminous and contained abundant hyaline casts and many leukocytes.

The right pleura was aspirated immediately and 45 ounces of a hemorrhagic fluid was removed, containing much flaky fibrin. It was odorless, opaque. On its examination at the Ayer Clinical Laboratory, by Dr. Longcope, showed many polynuclear leukocytes, numerous red blood-cells, and much fibrin; no ameba; cocci on staining; sterile on culture.

The fluid reaccumulated, and he was tapped on July 20th and 28th, August 8th, and September 18th and 27th, with the removal of 24, 35, 39, 112, and 48 ounces respectively. By August 8th the fluid was first noted to be reddish in color. It is described by Dr. Flexner as follows: A thick reddish-brown fluid, lighter colored gelatinous material forms on surface, with grayish-yellow fragments present. On microscopic examination, many fatty leukocytes, fat droplets, and a clear intercellular substance, in which are numbers of crystals of hematoidin or bilirubin. Some few larger cells found which were not unlike liver cells; no ameba.

The blood-count on July 27th was as follows: Erythrocytes, 3,140,000; leukocytes, 10,000; hemoglobin, 35 per cent. On August 9th: Erythrocytes, 3,190,000; leukocytes, 8000; hemoglobin, 30 per cent.

The liver increased in size and became very tender. His temperature was irregular; his strength failing. On August 18th he developed the signs of a pyopneumothorax, and coughed about one quart of material similar in character to that aspirated.

He persistently refused operation. The stools from the beginning were formed and normal in appearance; no ameba were searched for in them.

A few days before death a leukocytosis of 21,000 developed. Death occurred on October 1st from cardiac exhaustion.

Autopsy, by Dr. Longcope, October 2d, fourteen hours after death: The body of a large negro, somewhat emaciated, 167 cm. in length. Rigor mortis present. Pupils dilated; face edematous. On the prepuce of glans penis are numerous ulcerated areas, the larger ones being slightly raised, irregular, somewhat indurated, pale edges, while the bases are necrotic. The abdomen is distended; the subcutaneous tissues are edematous; muscles are quite pale.

Peritoneal cavity contains about 200 c.c. of clear yellow fluid. The liver is greatly enlarged and presents a nodular mass just beneath the xiphoid cartilage. In the mammillary line of the right side the liver extends 13 cm. below the costal margin; in mammillary line of left side the liver extends 12 cm. below costal margin. The falciform ligament is pushed to the left until it reaches 4 cm. on that side. Immediately at the costal margin in the mammillary line on the right is a small punctured hole through the peritoneum and into the liver. About this puncture are moderately firm adhesions, and adhesions extend over the liver at this point up to the diaphragm. Diaphragm on right side reaches to the sixth interspace; on left side to the fifth interspace.

Thorax. On cutting through the ribs on the right side a large amount of air escapes, and with it some dark brown fluid. The entire pleural cavity appears filled with thin material, which becomes paler, more grumous, and gelatinous nearer the costal pleuræ. Amount, 3500 c.c. The lung is not visible; the walls of the diaphragm, costal, and parietal pleura are covered with a shaggy, yellowish-white, gelatinous material of 2 cm. in thickness. Right pleural cavity is free from fluid. Pericardial cavity contains a small amount of clear yellow fluid.

Heart. Epicardium contains almost no fat except on the right ventricle. Bloodvessels are tortuous, but not perceptibly thickened. Heart's flesh is pale and firm. Mitral valve normal, as are the tricuspid and pulmonary valves. There is a slight thickening of the edge of the aortic valve, especially of the left and middle segments, and along the lines are several teeth-like vegetations, which extend to the corpus Arantii. There is no shortening of the valves.

Spleen. Old adhesions over the upper portion to diaphragm. The capsule is wrinkled and there are strings over the anterior surface. Small in size; consistence firm. On section of surface there are large numbers of prominent Malpighian bodies. The pulp is of a brownish-red color.

Kidneys. Both alike. Capsule comes away easily. Surface smooth and pale. On section, the cortex is cloudy. Glomeruli visible, red; general surface pale. In one kidney is a cyst the size of an almond. Pelvis dilated. Mucous membrane shows numerous small hemorrhages. The other kidney shows the same condition, besides a triangular pale area 1.5 cm. in diameter, in which the glomeruli are pale and without a hemorrhagic border. General consistence firm.

Lungs. The left lung is congested. The pleuræ smooth and show disseminated uniform ecchymoses. On section, there is marked congestion and some edema. Bronchi congested. Bloodvessels at base free. The right lung will be described in connection with the liver.

Liver. The liver is enlarged; the enlargement affects the right lobe especially, but the left lobe is also enlarged, and the general consistence is very firm. The surface is slightly irregular. The diaphragm is free of left lobe, but bound to the superior surface of the liver on entire right lobe. Occupying the superior half of right lobe of the liver is a large abscess containing gelatinous, hemorrhagic, and necrotic contents.

The circumference of the abscess is 9½ cm. It extends in the median portion of the liver within 3 cm. of the left lobe, and on the left side within 4 cm. of the right border. The thickness of the liver tissue between the abscess and the anterior surface of the liver on the middle is 12 mm.

The abscess has ruptured through the diaphragm by a jagged cavity, which measures 3½ cm. in diameter, and communicates with the right pleural cavity. The diaphragm itself is converted into a fibrous band with the intermingled areas of muscle. The pleura covering the diaphragm on the right side is the seat of a pseudomembrane consisting of necrotic purulent matter 5 mm. in thickness.

The hepatic abscess is surrounded by a fibrous capsule, averaging from 5 to 7 mm. in thickness, the inner surface being roughened and covered with necrotic purulent material. The right lung is bound to the pleura, and the left inferior border is compressed. The inferior visceral membrane is greatly thickened and covered with similar necrotic purulent material as that over the diaphragm. This necrotic material has perforated the pleura and is in communication with the bronchi. It can be pressed into the bronchi, and, on cutting up the latter, two communications of the inferior bronchi of the second order are seen to have taken place. In one of them are appearances indicating destruction of the bronchial wall, with the destruction of nearly one-half of it.

The cut surface of the lung is dark, congested, and shows little air.

Intestines. The small intestines appear normal. There are no ulcerations in the large intestines, but in the colon and cecum are a number of pigmented scars, varying from 4 or 5 to ½ or 2 cm. in extent. They are depressed and smooth in texture. One or two of them are elevated above the surface of the intestine.

Esophagus and stomach apparently normal. Pancreas and testicles apparently normal. Aorta smooth throughout its length. Mesenteric glands and retroperitoneal glands are much enlarged, forming grape-like branches beneath the pylorus. They are hard and lobulated. On section, they appear gray, smooth, and translucent. On removing the eyes the orbital tissue is found to be quite edematous. The brain is being hardened.

Amœba coli were demonstrated in the scraped abscess wall contents by Dr. Flexner; they were but feebly motile.

Points of Interest. Clinical: 1. Latent abscess, with no history of previous dysentery. 2. Sudden rupture into right pleural sac, with all the signs of acute hemorrhagic pleurisy. 3. Development and disappearance of a pyopneumothorax.

From the Pathologic Point of View. 1. The character of the pleural exudate: A thin brownish-red fluid, with a heavier brownish flocculent sediment, containing fatty leukocytic cells, looking like liver cells; bile pigment, fatty crystals, but no ameba, and sterile on culture. 2. The characteristic large single abscess in the right lobe, and its thick wall and viscid pus. 3. The very old lesion in the colon. 4. The curative powers of nature, which were well marked in this case, as seen in the extensive thickening of pleura, obliteration of the diaphragm, and the two attempts to get rid of the pus in her own way—*i. e.*, rupture through the diaphragm and rupture through the bronchi. *October* 24, 1901.

A Report and Exhibition of the Largest Recorded Aneurysm of the Heart.

ROLAND G. CURTIN, M.D.

Cardiac aneurysms, although in themselves of little clinical importance, nevertheless, on account of their rarity, are always interesting, and for that reason it is my desire to report the following case. I believe it to be unique in that a careful search through medical literature has failed to reveal any instance in which the aneurysmal sac reached the tremendous proportions of this one.

Two years before the patient came under my charge he was admitted to the Philadelphia Hospital with general dropsical symptoms. He was under my observation for two years. During this time and one year before his death Dr. Pepper decided that he had a left pleural effusion, and introduced an aspirating needle, drawing off 235 c.c. of pure blood, which rapidly coagulated. The case was reported by Dr. Pepper as one of hemothorax. No unpleasant symptoms followed the operation.

When the patient came under my care the whole of the left anterior chest, nearly to the axilla and clavicle, was pulsating and heaving with each beat of the heart. To the left of the sternum, at the junction of the fourth and fifth ribs, there was a circumscribed, more markedly pulsating area. He had attacks of dyspnea on slight exertion or when under excitement for two years before death, associated with a cyanosed condition of the skin, particularly about the face. He was also dyspneic when the atmosphere was heavy.

About two months before death the anasarca, which had disappeared two years before, returned, with increased dyspnea. During the last two years of his life his radial arteries had undergone rapid degenerative changes, so that at the time of his death these vessels were like a string of beads, from their atheromatous condition. During the last few months that he lived he became weaker and weaker, and death was looked for two days before it occurred. He died rather suddenly, apparently from apnea. At the time of his death his face was greatly swollen.

Physical Examination. On inspection a slow, outward wave toward the left was observed, which went far out beyond the left nipple, and high up near the left clavicle. Palpation showed that this heaving, wavy impulse extended as far out as the mid-axillary line and at times beyond it. On percussion the left side of the chest was found to be flat over its entire surface. Auscultation showed an absence of all breath or voice sounds. On applying the ear to the chest to the left of the sternum, at the fifth interspace, a long, rather soft, systolic murmur was heard, followed by a long, rather soft, whiffy sound, which corresponded in time with the diastole of the heart. The two sounds together occupied nearly the whole cardiac cycle.

Postmortem Examination. The following notes were taken at the time of death, when the postmortem examination was made:

"The *left lung* was compressed to about one-third of the size of an ordinary fist and pushed above the position of the root of the lung, where its apex should have been. The *right lung* was slightly compressed, as the heart encroached upon the right cavity of the chest. Here and there were emphysematous patches. The pleural cavities contained no effusions or adhesions and were healthy.

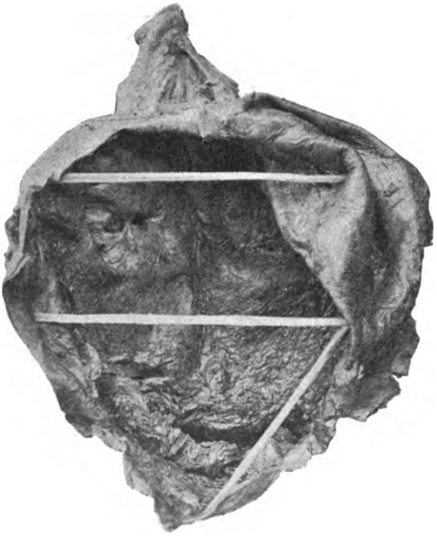
"The *heart* itself was hypertrophied, particularly the left ventricle. The aortic valves were slightly thickened and stiff. The mitral valve and the pulmonary valves were healthy.

"Springing from the left ventricle was a very large aneurysmal sac, which was in close contact with the left side of the chest. The pericardium was thickened and quite intimately adherent to the heart and the aneurysmal sac, but they could be separated by the occasional use of the knife. The mediastinal pleuræ were everywhere incorporated with the pericardium. Near the base of the heart the pleura contained soft, yellow lymph, evidently the result of a recent inflammation.

"The aneurysmal sac formed the apex of the mass. Its walls were about 0.3 cm. thick, and were composed of a dense, light, fibrous material, appearing to the naked eye to be made up of widely separated muscle fibers, demonstrable after the pericardium was removed.

"When the sac was opened it was found to contain a large amount of blood. In its lower part and half-way up its sides it was coated with laminated clots, about 2 cm. in thickness. After the removal of the black clotted blood the cavity was filled with water. Upon weighing its weight was found to be 2850 grams. On emptying the sac and reweighing it the weight was found to be 1370 grams less. As a cubic centimeter of water weighs a gram, it will be seen that the cavity had a capacity of 1370 c.c., or nearly a liter and a half.

FIG. 1.



Aneurysm of heart.

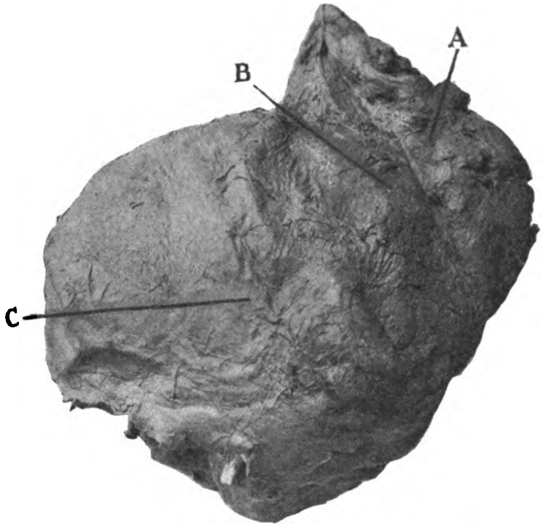
"Two holes, communicating with the left ventricle, were discovered. They were about the size of a large quill. The apertures were about 1.25 cm. apart, and seemed to be located in a white substance which was undergoing atheromatous change.

"The inside of the sac was here and there covered with plates of atheroma. In some places calcareous degeneration had taken place. Spicules of this material appeared in the incision, and at one place in the left side of the sac a hard plate gave forth a sharp click when struck with a knife.

"The *liver* was contracted, indurated, and congested. Its edges were contracted and rounded. To the right of the transverse fissure was a white spot, depressed, and looking like a cicatrix, probably an old infarction. The *spleen* was small, blue, and firm. The *kidneys* were congested, slightly contracted, and a little granular. The capsule was quite firmly adherent. There was no erosion of the vertebræ."

Realizing that the above notes, made many years ago, did not adequately describe the minute points of interest in this specimen, I asked Dr. David Riesman for a more systematic description of it, and he has most kindly furnished me with the following dictation:

FIG. 2.



A. Right ventricle. *C.* Aneurysm springing from left ventricle *B.* (Posterior view.)

"*May* 26, 1901. The specimen is that of a heart which has been kept in alcohol for nineteen years. The organ is very much enlarged toward the left side, on account of hypertrophy of the left ventricular wall and the presence of a large aneurysmal sac springing from the left ventricle.

"The chamber of the left ventricle is about normal in size, but the wall is greatly thickened; in the preserved specimen it measures more than 2.5 cm. in thickness. The columnæ carneæ are well marked and the papillary muscles very thick and strong. The mitral valve, on its anterior leaflet, presents a small sclerotic patch;

it is, however, perfectly pliable. The posterior leaflet is normal. The tricuspid orifice admits three fingers. The aortic valve presents nothing abnormal, except that on one leaflet, at its insertion into the aorta, there is, on the ventricular surface, a small, elevated ridge of atheroma. The aorta is of normal caliber, and has scattered over the intima a few calcareous plates. The coronary openings are patulous, although one is rather small.

"In a small funnel-shaped recess situated between the two sets of papillary muscles of the posterior mitral leaflet are two oval openings connecting the aneurysm with the ventricular cavity. One opening has its long axis transversely, and measures about 1 cm. in length and 0.3 cm. in width; the second is of about the same dimensions.

"The margins of both openings are smooth, and, so far as can be determined at the present time, have a glistening, fibroid character. This is particularly true of the inner opening On the ventricular surface these openings are separated by a bridge of tissue 0.6 cm. wide and 1 cm. long. On the aneurysmal surface the openings are large, somewhat funnel-shaped, and surrounded by fibrous tissue, slightly puckered. The outer opening is undermined and communicates with the ventricle by a third perforation, opening about 0.8 cm. to the outer side of the median line, in a recess formed between the corresponding papillary muscles belonging to the anterior and posterior mitral leaflets. This opening on the ventricular surface is oval, with its long diameter vertical to the wall of the ventricle, and measures 1 by 0.3 cm. There are thus three openings on the ventricular surface, and two on the aneurysmal. They are all situated about 3.75 cm. from the auriculoventricular ring.

"The aneurysm itself is the size of a child's head, and springs from a point almost opposite the ventricular septum. It has thick, tough, fibrous walls, that can be separated into at least three layers. Where not covered by clot the internal surface is quite smooth and glistening. There are thick, laminated clots at the bottom of the sac, around its attachment to the ventricle, particularly at a point corresponding with the apex of the ventricle. The sac has been incised by a long, vertical cut, and shows no point of rupture. There are some signs of old adhesions on the external surface, especially at the base of the attachment of the sac to the wall of the heart. At its base the sac measures 15 cm. vertically and 13.75 cm. transversely; while from the ventricular wall, externally, to the inner wall of the sac the distance is 16.25 cm.

"To the outside of the openings is a crescentic, projecting ridge, forming a little niche about 2.5 cm. deep and 5 cm. high. This ridge is continued below as a low elevation for a distance of 5 cm. to a point 2.5 cm. below the openings.

"The chamber of the right ventricle is not enlarged. The wall measures about 1 cm. in diameter. The right auricle presents nothing abnormal. The pulmonary and tricuspid valves are normal. The foramen ovale is closed. The left auricle is normal.

"As the heart is at present, it having been somewhat flattened in the jar, it would appear that the apex was in a large degree constituted by the aneurysm."

There are three points of interest in this case:

1. So far as I am able to learn, it is the largest aneurysm of the heart that has ever been recorded.

2. The patient lived for years, not only with greatly diminished breathing capacity, but also with a severe complicating cardiac condition.

3. The removal of 235 c.c. of blood, to accomplish which must have caused a break in the continuity of the aneurysmal walls, failed to produce any symptoms whatever.

November 14, 1901.

A Case of Anemic Necrosis in the Wall of the Left Ventricle Above the Apex of the Heart Associated with Angina Pectoris and Locomotor Ataxia.

ROLAND G. CURTIN, M.D.

The case is that of a practising physician, fifty-four years old, who was working hard in a country practice. Fifteen or twenty years ago Dr. D. Hayes Agnew said that a sore on the index finger was undoubtedly a chancre. No positive evidences of secondary or tertiary syphilis were observed. He had had mild symptoms of angina pectoris for the past three or four years, which gradually grew worse until, in October, 1899, he could scarcely walk, owing to the intense suffering. He had lightning and girdle pains, and was unable to walk in the dark, and in the daylight it was necessary for him to keep his eyes on the ground.

At the time that I examined him with Dr. Stokes there was no abnormal pulsation of the heart; no bruit, thrill, or murmur. Both pleural cavities contained fluid. After great suffering, he died about two weeks later. In January, 1900, Dr. Stokes reported to me that soon after I saw the patient he grew much worse. He had oppression and increased dyspnea; a violent form of Cheyne-Stokes respiration set in, the lungs became congested, and the legs were paralyzed. After lingering about six days, he died in great distress.

The autopsy showed effusion in both pleural cavities and recent adhesions on the right side. There was hepatization of the middle lobe of the right lung and part of the lower lobe of the left, and effusion and recent adhesions in the pericardium. The inner surface of the pericardium was quite rough. The heart was large, weighing 468 grams, with soft, flabby, muscular walls. An organized clot was found in the right auricle. The coronary arteries were extremely rigid, and grated under the scalpel like plaster. In the distribution of the anterior coronary artery, near the apex, a cavity of *anemic necrosis* was found, holding about 15 c.c. of a chocolate-colored, semi-fluid substance.

The specimen illustrates how an aneurysm could result by the rupture of such a cavity into the ventricle; or should both walls give way, causing a communication between the ventricle and the pericardial sac, a complete rupture of the heart would naturally be the result. *November* 14, 1901.

A Case of Interventricular Aneurysm Opening Into the Right Ventricle by Ulcerative Process, and Aneurysm of the Abdominal Aorta.

ROLAND G. CURTIN, M.D.

History: January 9, 1885. Matthew Daly, aged fifty-three years, single, white; born in Ireland; came to America when three years old. Has used whiskey and beer to excess and tobacco moderately all his life. Has always had fairly good health. Had measles when a child, and chills and fever six years ago. Has never had rheumatism.

In 1875 he had a primary sore, which was followed by no secondary symptoms. Five years ago he had a severe fall from a horse. He first noticed palpitation of the heart and shortness of breath three years ago, but considered himself perfectly well, except for some precordial pain, until March, 1884. At that time he was seized with an attack in which he became very faint, fell down unconscious, and remained so for several minutes. On attempting to get up, some three hours later, he found himself still very weak. He did not have another attack until March, 1885. This attack lasted about an hour, with a period of unconsciousness of probably ten minutes. At this time he vomited, but on no occasion did he expectorate any blood.

Since the date just mentioned he had a number of attacks, which seemed to be becoming frequent, although they were apparently not more severe than at first.

Physical examination shows that the precordia is prominent and bulging. There is a very apparent area of pulsation, 5 cm. in diameter, in the third interspace, between the mammary line and the left border of the sternum. The apex-beat is visible within the nipple line, and extends over an area which would correspond to a circle with a diameter of 3.75 cm.

Over the pulsating region, as above given, is heard a systolic murmur, most intense over and above the second costal cartilage, at a point midway between the nipple line and the left border of the sternum. Palpation shows that there is also present a marked thrill.

The patient also complains of a sharp pain shooting through to the back, which, from the murmur also present here, probably has its origin in the abdominal aorta.

Note, *November* 20, 1885. The patient is now suffering from one of his attacks. He feels faint, and his whole body vibrates with each systole of the heart. The pulse is 136, and gaseous, small, and feeble. He states that at the beginning and close of his attacks his eyesight fails and his eyeballs become more prominent.

Autopsy, March 26, 1886. All notes made at autopsy not directly bearing upon the physical signs are omitted.

Left thorax, prominent up to the upper border of the second rib, extending over the entire heart region. Pericardial sac bulging. Precordial space full and entirely uncovered by lung. Thoracic aorta slightly dilated; there is a small, saccular dilatation above its origin anteriorly, capable of admitting a small chestnut. Inner surface roughened with some calcified plates on the arch.

Heart. Left auricle much dilated; mitral orifice dilated, admitting more than three fingers; valves slightly thickened. On opening the right ventricle an aneurysm of the undefended portion of the interventricular septum is found bulging into the right ventricle, into which it opens through a small orifice, probably the result of an old ulceration. This aneurysm is large enough to contain a good-sized walnut. The right auricle is also dilated.

The abdominal aorta is much thinned at its commencement, and throughout its entire length is the seat of extensive atheromatous changes. Extending from the diaphragm to the iliac arteries is a fusiform aneurysm filled with old coagula, its lumen being occupied by recent clots. There is no erosion of the vertebræ.

The liver and kidneys show considerable passive congestion.

November 14, 1901.

Proceedings
of the
Pathological Society of Philadelphia.

DECEMBER, 1901. NEW SERIES, VOL. V., NO. 2.

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Presidential Address.

FREDERICK A. PACKARD, M D

FOUR days from now this Society will have completed its forty-fourth year of life, it having been organized on October 14, 1857. When the Constitution was adopted the following officers were elected:

President,	DR. GROSS.
Vice-Presidents,	DRS. LA ROCHE and STILLÉ.
Treasurer,	DR. ADDINELL HEWSON.
Secretary,	DR. DA COSTA.
Assistant-Secretary,	DR. T. G. MORTON.

No time seems to have been lost, as the minutes appearing in the TRANSACTIONS, after briefly giving the above facts, state that the Society then proceeded to the exhibition of specimens, the first one being shown by Dr. S. Weir Mitchell. The membership list given in the first volume of the TRANSACTIONS, which covered the period from the time of the organization of the Society up to May, 1860, included sixty names. Of these original members but eleven are still living. Of the original list of members, but four are found in our present reports; two, Dr. Da Costa and Dr. Stillé, having died since the completion of the last report. Seven additional original members are still living, although their names no longer appear in our list of membership. They should certainly never have been allowed to resign, but should have occupied a place of honor on our rolls.

The Philadelphia Pathological Society was founded eleven years after the corresponding society in London, the first meeting of that body having been held on the 16th of November, 1846. From the character of our proceedings and the way in which they were published, I judge that the Philadelphia Pathological Society took for its model its London predecessor, possibly one source of our continued usefulness. As far as I can find, but one pathologic society in this country had preceded ours. In Volume I. of the *Transactions of the New York Pathological Society*, which was published in 1876, a history is given of that association. According to it, the first meeting was held on June 14, 1844, although the publication of the printed *Transactions* was delayed until 1876. In 1881 "The Chicago Pathological Society" was the name adopted to designate what had previously been known as "The West Chicago Medical Society." Its first volume of *Transactions* appeared in 1896. Within the last two years a national association of pathologists has been started. It is seen that, while we were early in the field, two other societies with the avowed purpose of studying pathology were in existence before ours was founded.

The first president of the Society was Dr. Samuel D. Gross, whose election to the office was a favorable omen. The pioneer work of Gross in the field of surgical pathology has more than justified his selection as the first president of a society devoted to the subject of pathology. The work of Stillé is, of course, well known to all of us, some of whom listened to his lectures from the benches. His contributions to medicine are very many, and all have a distinct value. For the three years from 1864 to 1866 the meetings of the Society were presided over by Dr. J. M. Da Costa, whose subsequent wide-spread reputation as a diagnostician was undoubtedly due in great part to the pathologic work which he performed in his earlier years, evidence of which frequently appears in the earlier volumes of our TRANSACTIONS. Dr. John Ashhurst, Jr., who also has so recently died, was the president of the Society in 1870. His name also is one which enhances the brilliancy of the list of former presidents. A close associate of Dr. Ashhurst was the next president, Dr. James H. Hutchinson. Many of us at present active in the Society had the privilege of being associated with Dr. Hutchinson as resident physicians in the hospitals in which he was visiting physician. While never widely known as a pathologist, Dr. Hutchinson's success as a practitioner of medicine was certainly in great part due to his early interest in pathologic matters. The president succeeding Dr. Hutchinson was Dr. William Pepper, usually termed the younger, but better known as William Pepper, Jr., inasmuch as his son of the same name is also now an active member in our Society. Of Dr. Pepper's attainments far abler pens than mine have written, and the active influence which he had for many years upon scientific medicine is still felt with such force that no further words are necessary in enumerating the proud record of the Society in its presidents. Dr. H. Lenox Hodge was elected president in 1876, succeeding Dr. Pepper. While better known as a gynecologist and obstetrician than as a pathologist, his work doubtless was made more thorough and valuable by his familiarity with pathologic processes. Dr. S. W. Gross was elected president in 1879. His intimate acquaintance with pathology, doubtless stimulated by the example of his father, appears in all his surgical writings, especially in connection with malignant disease of the breast. The next president whose name appears on the list among those whom we are unfortunate enough not to still have with us is Dr. E. O. Shakespeare, whose work upon Asiatic cholera is such a monument of his industry and ability that had that been all he had contributed to medicine it would be sufficient to make us proud to have chosen him for a former president. Following two others who fortunately are still living, the name of Dr. Henry F. Formad appears as the last of those of our presidents who have died. Those of us who had the fortune to receive instruction from Formad in gross pathologic anatomy in the laboratory will fully realize that he contributed his share to the advancement of pathologic interests in this city, while no one can forget his vivid description of the many interesting finds which he brought before the Society when he was Coroner's Physician.

In our list of members published from year to year in our TRANSACTIONS it is interesting on looking over the past volumes to notice how thoroughly each of the main divisions of the practice of medicine and the specialties are represented. The Society never has been, and it is to be hoped never will be, a society purely of pathologists. I think it will be conceded by all, whether they be active members of the Pathological Society at the present time or no, that of all the numerous societies that have existed or still exist in Philadelphia not one has had such an important influence on medical thought in Philadelphia as has the Pathological Society. The reasons for this are quite obvious. Among the attendants at the meetings there have always been a fair proportion of men paying special or even undivided attention to pathology, and also of men who have been interested in pathology as a science until their practical work at the bedside in hospital and private practice made its further active pursuit impossible. Others there are who take time from a busy practice, which gives but little opportunity for pathologic work, to come to the meetings and hear what others have to say and see what specimens have been obtained by those whose charitable or teaching positions give them opportunities which this class can themselves not obtain. Most of us who have become faithful attendants at the meetings of the Society usually joined it while resident physicians in one of the hospitals. The seeing of specimens, the hearing of papers and discussions are doubtless the best incentives that any of us can have toward keeping in touch with pathologic work. Fortunately, there are usually at the meetings a large number of men of clinical experience, so that questions in pathology are usually discussed more in connection with their bearing upon the practice of medicine and surgery than in a purely scientific direction.

I do not doubt that those who started the Pathological Society wondered whether it would be possible to maintain interest sufficient to warrant the starting of such a special association. They certainly could not have anticipated what a tremendous influence the Society started by these forty men would have upon Philadelphia medicine, and that the membership would have steadily increased until in the present year it numbers 292. Undoubtedly, also, they did not realize that the Society which they were founding would be made the model for other societies started in the city. Many of us know that when new societies have been started in Philadelphia within recent years the method of organization adopted has been that found useful in the Pathological Society, and everyone feels that the nearer the workings of the new society can be made to correspond with the methods employed by the "Path" the more assured will success be. There is no doubt that part of the success of the Pathological Society can be attributed to the absence of politics in its government. Whatever the cause may be, it is, I am sure, realized that no society in this city has the affection of its members, either active or passive, as has the Pathological Society. I imagine that this is in great part due to the fact that a man usually joins shortly after graduation; that at its meetings he hears discussions, sometimes animated, but always friendly, upon subjects which cannot fail to interest one truly earnest in his profession. At the semi-annual conversational meetings he hears a paper from someone with whose name he is familiar and upon whose reputation he has probably looked with a considerable amount of awe. After the conversational meeting, and to a less extent after the other meetings, he learns to know men somewhat older than himself who may eventually become his life-long friends.

Fifteen years is not a very long time in the life of such a society as ours, yet it is interesting to me to see the changes that have occurred in this Society since I joined it in 1885. In that year Dr. Shakespeare was the President, and I remember with what anticipation I came to my first meeting and saw sitting on the benches some of those who have taught me what medicine I knew and others whose names I had heard as prominent in the profession. I very distinctly remember the first specimens I presented, after much urging by Dr. Osler, who was then my chief in the University Hospital. The dread with which I looked forward to hearing my own voice was much diminished when I found that I was speaking to men who evidently would not be hypercritical, and yet who seemed interested in the very unimportant and ordinary specimen which I presented. The very fact that many of us have made our first dive into the reading of medical papers before this Society is probably one reason for its holding its members for so long a time. Certainly the reading of papers before this Society seems easier than before many others, and has given us confidence because of our having safely accomplished our first endeavor at these meetings.

It is interesting to go over the old numbers of the TRANSACTIONS of our Society and see how constantly the character of the specimens exhibited has kept pace with the questions which at the time have been to the fore in medicine and in pathology. I think that we can congratulate ourselves upon the fact that the same thing is true at the present time. Apparently our meetings have for the past few years been fully as well attended as at any previous time, and I am sure that the discussions are equally interesting. In some respects, unfortunately, lately the material announced on the program has been so large that, in spite of the best efforts of the Business Committee to devise ways for facilitating the work of the evenings, there is, I feel sure, an unwillingness to enter into discussion because of the feeling that our time is already overcrowded. In some ways I think that this is a pity, because the hearing of the discussion of others undoubtedly stimulates pathologic thought.

Recently I have been looking over some of the early volumes of our TRANSACTIONS, and have been struck with two facts. The first of these is the excellence of the work which has been constantly brought before the Society by our predecessors. The second is the remarkable contrast which exists between the type of subjects discussed at the meetings in 1857 as compared with those occupying attention at the present time. Not only pleasure but a great deal of profit is to be obtained by looking over our old volumes. The care with which the clinical manifestations and the lesions in the organs were studied could not be surpassed, while the discussions upon the papers are well worthy of careful perusal, as they are characterized by earnestness and thoroughness. Another feature of the early reports which rather impressed me was the fact that very frequently the statement is made that a particularly interesting patient had been seen by several members of the Society, sometimes in consultation, but frequently apparently from the desire of one friend to show another an interesting example of an unusual disease. I think that at the present time such invitations to others to observe our interesting cases might be of decided advantage.

A few years ago a complete index was published covering all of the papers appearing in our proceedings from the time of the foundation of the Society. A recapitulation of our records would therefore be useless and tedious. I would, however, like to draw attention to some of the main features exhibited by the first volume of our TRANSACTIONS, in order to compare them with the papers that we have had brought before us during the past year. Forty-three years is not a very long time in the history of medicine, yet a comparison of the work done at that time and at the present shows in a striking manner the advances in medicine that have been made in the past few years. I think, however, that we have possibly lost a little too much of the vivid clinical descriptions that evidently were an important part of the meetings during the first years of the Society. In the first volume of our TRANSACTIONS there are many papers upon subjects which we too infrequently see before us at our meetings at the present time. I refer to specimens of diseases of bones and joints. A few years ago a series of joints from a case of rheumatoid arthritis were presented before the Society and created a great deal of interest among the members present. So far as I can remember this was the only meeting at which I have seen presented instances of this disease, although it cannot be said that we as yet know so much about it that further study is by any means unnecessary. Specimens of tumors were far more frequently shown in those days than at the present time, a fact that I think can be readily accounted for by the large amount of fruitful study which has been given to these growths since the time of the appearance of our first volume. The classification of tumors at the present time is much more well defined than it was then. Within the last few years we have had presented at our meetings quite a large number of specimens of cancer of the head of the pancreas, a lesion that is now far more frequently ascertained during life than at one time was the case. One of the most important contributions to our knowledge of cancer of the pancreas, and one which is still quoted in every systematic article upon the subject, appeared in our first volume of the TRANSACTIONS. At the second meeting of our Society, Dr. J. M. Da Costa showed a specimen of primary cancer of the pancreas, which in the next year was made the basis of an elaborate, careful, and extremely valuable report upon this disease, accompanied by a table analyzing thirty-seven instances of a similar condition, one of the thirty-seven, besides the one forming the subject of the paper, having also been reported in this same volume of the proceedings by Agnew. A curious case of cyst from the liver coughed up through the pulmonary passages was also exhibited that year, and it is interesting to see in reading over this paper how many more ways of investigating such a case we have at the present time than were at that time available.

Another subject that at the present time is causing considerable discussion is cirrhosis of the liver with diabetes. An example of this association was presented in 1857 to the Society by Dr. Morton, with interesting remarks by Drs. Da Costa and Forbes. An observation suggested by a paper read before the Society by Dr. Harris upon the subject of variations in the position, form, mobility, vascular connections and arrangement of the excretory ducts of the kidney, is that so frequently men who took part in the proceedings of the Society showed by their contributions that their knowledge of medicine took a wide range before they finally became well known in some particular branch. Dr. Harris, as we most of us know, is now chiefly remembered from his valuable statistical work concerning various abdominal operations, yet his paper upon malformations of the kidney is one that would do credit to an anatomist. Others whose articles appear in the first volume of the TRANSACTIONS, the subject-matter being of general pathologic interest, have later become well-known specialists or active practitioners in far different fields from those indicated by their first papers, and doubtless they have become well-known specialists or successful practitioners in great part because of the range of their observation in their earlier years when they were active members of the Pathological Society. A rare specimen of gangrene of the spleen was reported by Dr. Hall, afterward one of the surgeons of the Wills Eye Hospital. A few years before he left Philadelphia he talked to me about this specimen and this report in as enthusiastic a manner as though the practice of ophthalmology had not weaned him from his old love of general morbid anatomy.

Addison, in 1855, published his observations on the constitutional and local effects of disease of the suprarenal capsules. The subject, therefore, must have been of absorbing interest, because of the recent recognition of the connection of adrenal with bronzing of the skin, when Da Costa, on October 15, 1858, presented a specimen of cancer of the liver and suprarenal capsules without bronzing of the skin. The frequent absence of this sign in cases of malignant disease of the suprarenal capsules is now, of course, well recognized, but it is interesting to note that in the discussion upon Dr. Da Costa's paper Dr. Mitchell "spoke of the frequent absence of the peculiar color in cases of cancer, and suggested that there might be, as it were, two sets of cases, one with and one without these symptoms." It seems rather curious to us at the present time to see on page 58 of the first volume of our TRANSACTIONS the results of the examination of two cases of black vomit, apparently from yellow fever patients. An opportunity to see a specimen of this kind would rarely occur to any of our members at the present time. Among other interesting features of the first volume is the exhibition of a specimen of aneurysm of the subclavian artery into which perchlorid of iron had been injected, not, however, by the member showing the specimen. The report of a case of congenital fissure of the sternum, studied by Dr. Da Costa with great care, is well worthy of careful reading. The heart was uncovered by bone over a sufficient extent to allow very interesting observations to be made in regard to the sounds produced at various points. On page 275 is a small notice which accompanied the exhibition of a drawing of elastic tissue found in the sputum of a phthisical patient. The author, Dr. Darrach, speaks of the value of the microscope in diagnosis in doubtful cases of pulmonary affection, a striking evidence of the advances in diagnostic means afforded to us by the study of bacteriology.

In glancing over our last completed volume certain points of contrast stand out prominently, a few of which may be mentioned. A specimen was shown of endothelioma of the retroperitoneal space. Such a designation of a tumor would have had absolutely no meaning in 1857. The work on experimental pancreatitis, which was recorded in recent numbers, is in an entirely new field. The subject of experimental pathology occupies quite a considerable amount of our proceedings at the present time, and is a method of research which occupied no place in the earlier meetings of the Society. The Widal reaction is frequently mentioned, a clinical help, which has only come to us within very recent years. An article on anthrax reminds us that the etiologic factor of this disease was described shortly before our first volume of TRANSACTIONS was printed, yet it was many years before the subject of bacteriology was put on such a footing that it was of value either to the science of pathology or to diagnosis. The distinction between sarcoma and carcinoma, which is so frequently seen in articles in recent years, has all come about since the foundation of our Society.

Articles upon malaria are now filled with terms which in the earlier days of our Society had no meaning, Laveran's discovery of the plasmodium in 1880 having marked a distinct epoch in our knowledge of the disease. In a recent volume, also, there appears an article having to do with the use of antistreptococcic serum, a subject far from the thoughts of the originators of the Society. Another article within the last year deals with venom and antivenene, a subject in which interest was first created through the work of Dr. S. Weir Mitchell, who was one of our original members. Last year trichinosis was the subject of a paper at the conversational meeting, being delivered by Dr. C. W. Stiles, of Washington. It reminds us that the significance of the trichina as the cause of disease in the human being has only been realized since Zenker's publication three years after our Society had its birth.

A glance at former volumes is, I think, of great moral value to us. We are accustomed to feeling that we are doing much better work now than was ever done before in medicine. If we glance at the old volumes we find clinical descriptions unsurpassed, capacity for observation fully equal to that of the present time, deductions from observed facts carefully drawn, and an earnestness in discussion which cannot but impress one with the fact that forty-three years ago the work of the members of the Pathological Society seems no more behind the times than it is to be hoped our work will seem in the year 1944.

According to the By-laws, the duty of the President at this meeting is to summarize the work of the year and to make suggestions as to future plans. I have exceeded the prescribed duty in that I have ventured to speak a little concerning the impression made by fifteen years of membership in the Society and to touch upon some of our early history. In order to accomplish my duty of the evening, I would, then, at this late date turn over a new leaf and perform the duties directed by the By-laws.

During the year there have been nineteen meetings, the average attendance at which numbered thirty-five. This I consider a very satisfactory showing. A special discussion upon certain questions connected with diabetes was held on January 24th. The attendance at this meeting was fifty-three members, and the meeting was eminently successful in the interest that the papers excited. On April 27th we held our annual conversational meeting, at which

Dr. C. W. Stiles, of Washington, delivered an address upon trichinosis and trichina inspection. As would have been expected from such high authority as Dr. Stiles, the paper was full of interest. A novelty which was introduced this year, after serious consideration by the Business Committee, was the holding of a general exhibition meeting. On December 13th the floor of the Mütter Museum was used for the exhibition of a large number of gross pathologic specimens and microscopic preparations. This meeting was an experiment, but one that proved far more successful than was expected by the most sanguine. Not only were the specimens seen by a large number of men, but those of us who were anxious as to the result were extremely gratified at the expressions of opinion as to the value of the exhibition which were heard at the time and afterward. It seems to me an experiment worth repeating.

In regard to suggestions for the future, I can do no more than say that if the Pathological Society continues to do as good work in the future as it has done in the past, no more can be expected of it.

In closing, I wish again to thank the Society for the high honor that they have conferred upon me in selecting me to preside over its meetings for the last two years. Being in intimate touch with the affairs of the Society has been a source of great pleasure to me, while I shall always feel that in having been one of the presidents of the Pathological Society I have had conferred upon me an honor of which anyone might well be proud.

October 10, 1901.

A Contribution Concerning Creatinin Excretion.

DAVID L. EDSALL, M.D.

(*From the William Pepper Laboratory of Clinical Medicine, Phœbe A. Hearst Foundation.*)

This report is based upon the results which I obtained in estimating the creatinin excreted in the urine in a case of family periodic paralysis under the care of Dr. John K. Mitchell. The reasons for estimating the creatinin were partly the clinical nature of the case and partly as follows: I was asked to determine whether or not there was any evidence of acid intoxication in the case, and consequently searched for oxybutyric acid (the crotonic-acid test), acetone, diacetic acid, and lactic acid in the urine, determined the alkalinity of the blood during an attack and in the interval, and determined the excretion of ammonia throughout a series of attacks and the corresponding intervals. The results were all negative as to any evidence of acid intoxication, but the ammonia excretion showed a remarkable reduction (down to 100 mg. or less per day) for several days preceding the attacks, and rose to about one gram with the onset of the attacks or shortly after their appearance. Since the excretion of ammonia is an index of the amount of acids being formed and excreted, and since it is probable that the muscles play a considerable part in the production of acids in the system, the condition of the ammonia excretion before the attacks suggested the possibility that there is in this disease a decided qualitative or quantitative change in muscle metabolism which precedes the attacks and perhaps causes them. There is also the possibility that the excretion of ammonia was reduced because that of other alkalies was increased. This possibility is compatible, however, with the view that the low ammonia excretion was an index of alteration in muscle chemistry, for the excretion of potassium in particular is largely influenced by the condition of the muscles. The most satisfactory way of determining whether there were decided alterations in the chemical activity of the muscles at the times when the ammonia excretion was low seemed to be the determination of the creatinin excretion, for so far as our present knowledge of creatinin excretion reaches it indicates that it varies chiefly in relation to the condition of the muscles, excluding those variations which are due purely to diet. Creatin, from which creatinin is formed, is found in small amounts in various tissues, but is probably produced in notable amounts only by the muscles and the thyroid gland, and by the muscles in far greater amounts than by the thyroid gland. Creatin is found in very large relative quantities in the muscles, and the amount is greater if the muscle has recently been functionating actively. Further, active muscular exercise increases the excretion of creatinin. (There is some contention over this point, but I believe that the more recent work by better methods justifies this statement.) Extensive muscular paralysis and other pathologic conditions associated with marked lessening of the functions of the muscles decrease the excretion, while during actual wasting of the muscles the amount is increased. It has recently been claimed by Gregor that the excretion of creatinin is a direct index of the condition of muscle metabolism. While all the facts mentioned indicate a very evident relation between the excretion of creatinin and the activity of chemical changes in the muscles, some isolated observations tend to show that creatinin excretion may vary decidedly in accordance with other changes than those in muscles, and it cannot be said that Gregor's contention is wholly justified. But it may be said that the excretion of creatinin is more nearly an index of the condition of muscle chemistry than is the excretion of any other substance, so far as known, and there can be little doubt that some part of the excretion of creatinin, at any rate, is intimately dependent upon the chemical processes occurring in muscles. It is claimed by certain authors that the creatinin excretion in the urine is wholly dependent upon the character of the food; there is, however, no reasonable support for such a view, and there is good evidence against it.

I estimated the creatinin by the Neubauer-Salkowski method, continuing the ammonia estimations throughout the attacks in which the creatinin was estimated, and also determining the total nitrogen of the urine (Kjeldahl method) as a check upon the amount of nitrogenous food being taken. The man's diet was kept uniform during the intervals, but it was impossible for him to take the usual amount of food during the attacks. This fact, however, makes little difference in interpreting the results which I report, since the main changes to which attention should be directed occurred before the attacks, at the period when he was taking the usual amount and kind of food. The excretion of ammonia showed no changes of importance, excepting as already indicated. The excretion of creatinin and nitrogen was as follows:

		Creatinin in grams.	*Nitrogen in grams.*
March	29	0.0879	18.942
"	30	0.1482	
"	31	0.0561	19.820
April	1	0.1131	13.958
"	2	0.0819	14.490
"	3	0.5599	20.677
"	4	0 8879	20.506
"	5	0.1538	20.930
"	6	0.1819	19.257
"	7	0.0749	22.242

		Creatinin in grams.	Nitrogen in grams.
April	8	0.0117	23.068
"	9	0.4927[1]	11.340[1]
"	10	0.0795	17.052
"	11	0.1123	21.873
"	12	0.0499	17.606
"	13	0.0936	20.888
"	14	0.2019	20.508
"	15	0.2496	18.860
"	16	0.2247	19.152
"	17	0.1053	20.124
"	18	0.0140	18.043
"	19	0.0280	18.866
"	20	0.0031	13.333
"	21	0.0210	19.025
"	22	0.3838	15.650
"	23	0.1404	18.547

During this series of estimations the attacks came on as follows: On March 31st, lasting until late in the day following (April 1st); on April 8th, lasting through April 9th, and on April 19th, lasting through April 20th. It may be seen that preceding each of these attacks, and in the first and last instances throughout the attack, the creatinin excretion, which should normally be from 0.7 to 1.4 grams, was very greatly reduced, the amounts on several occasions being so extremely small as to be almost indeterminable, and throughout these periods being strikingly small. During the second attack, and immediately after the first and third attacks, the amount rises decidedly, the quantity found after the first and second attacks approaching the normal. It is important to observe that the low figures in each instance precede the onset of the attacks by several days, and that the reduction in excretion is, therefore, not due to the attacks. The relation to the periods of paralysis is very striking. The prolonged period of freedom from paralysis between the second and third attacks and the rise in creatinin excretion during this period seem at first to show that in this instance, at least, the relation of the creatinin excretion to the attacks was not so close as the other figures would indicate. In reality, however, the conditions during this time seem to offer even stronger evidence that the relation is a close one, for with the unexpectedly early rise of the creatinin excretion came an unexpected prolongation of the period of freedom from paralysis, and it was only when the excretion had fallen again to a very low point that the paralysis came on. The interval between attacks was, except in this instance, almost regularly seven or eight days. In this instance it was thirteen days. Another interesting fact is that the rise in excretion after the third attack was comparatively slight, and lasted only a short time, and that symptoms of an approaching attack came on several days earlier than usual (on April 24th). The last estimation of creatinin was made on April 23d, and I cannot state the conditions of excretion on the 24th or subsequently.

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[1] The figures for April 9th are too low for both the creatinin and the nitrogen. A portion of the urine was sent to Dr. Flexner, who investigated its toxicity. My figures are for the amount of urine that I received. Reckoned for the whole amount the figures would be: creatinin, 0 68 gram; nitrogen, 14.968 grams. I used the figures given in the table because the amount sent Dr. Flexner was fresh urine, not an aliquot part, and it could not therefore be properly reckoned with the other.

The conclusions that may be drawn from this work are difficult to state. The close association of creatin and creatinin with muscle metabolism and the general clinical aspects of the case make it seem at first thought probable that the results obtained indicate some qualitative or quantitative disturbance of the metabolism in the muscles, more probably a qualitative change, and that there is an accumulation of normal or abnormal toxic products which finally results in an attack, a series of changes closely analogous to those observed in the uric acid in typical gout. A fact which lends some further probability to this view is Dr. Mitchell's experience that in one other case of periodic paralysis, and to some extent in this case, a potassium salt (the citrate) seemed to prevent the attacks or to lessen their severity. The muscles contain large quantities of potassium salts, which is evidence of the importance of potassium in the functionation of muscles, and the work of Biedermann, Ringer, and others has shown that potassium salts have at times a very active excitant action upon muscular contractions, even when the contractions have ceased under the influence of other inorganic salts. Loeb's recent work has demonstrated still more clearly the marked influence of potassium upon the muscles, and though it is evident that sodium, calcium, and other salts are necessary for proper muscle function, the potassium salts are peculiarly active. It is also known that in wasting of muscles and in overexertion potassium salts are lost in large amounts, while in wasting of other albuminous tissue the sodium salts suffer more markedly than the potassium.

Possibly additional evidence of the truth of the view mentioned may be found in the fact that active muscular exercise sometimes seems to postpone attacks in subjects of this disease, and in other cases to precipitate attacks. In other words, increase in muscular function has a marked influence upon the attacks. It is, of course, impossile to exclude the influence of the nervous system in the latter connection; and, indeed, if the view that muscle metabolism is at fault be correct, we must confine ourselves to the belief that it is the immediate cause of the attack, and not the primary cause of the whole condition, for there must, of course, be some disturbance antecedent to such a supposititious disturbance of muscle metabolism.

I am, however, unwilling to state that these results indicate a disturbance of muscle metabolism. I feel that it is quite possible that such a disturbance occurs in these cases, and believe that this is the readiest and apparently the most reasonable explanation of my results. But there are several possible arguments to be offered against this view. One or two objections can be disposed of quickly. In the first place, it might be thought that the reduction in the amount of creatinin or creatin-producing food had given rise to the results. Such a criticism, as I stated before, I cannot consider of importance, because the most striking reduction of creatinin excretion occurred before the attack, at a time when the man was taking normal mixed diet, and when his urinary nitrogen was maintaining the normal level. Another possibility—*i. e.*, that creatinin was present in the urine in the usual amounts, but had not separated out as crystals of creatinin-zinc-chlorid—must be thought of, since this occasionally occurs with this method for reasons that are not well known. The low figures which I obtained made me suspect this, however, and I tested the filtrate qualitatively for creatinin by Weyl's and Jaffé's methods, and obtained only a faint reaction or none at all. A slight reaction is practically always obtained when there is any complication in the use of the method, and hence this error seems to be excluded. It might also be thought that alkalinity of the urine had transformed the creatinin into creatin, and that the low results for creatinin were due to this. I tested the urine regularly, however, and found it constantly acid. The results, therefore, must be accepted as they stand, and the difficulty is only in the interpretation of their meaning.

The chief objection to the view that they indicate solely a disturbance of muscular metabolism is that this man was taking meats in moderate quantity at the times when his creatinin excretion was lowest. Hence, he should have been excreting larger quantities of creatinin than he did, unless there was general disturbance of metabolism. In other words, the figures which I obtained, while they are so small as to indicate with much probability that there was disturbance of muscle metabolism, are so exceedingly small as to indicate strongly that something unusual must have been happening to the creatin or creatinin furnished by the food—*i. e.*, that there was probably some disturbance of general metabolism also. I think, therefore, that the only conclusion justified by the results obtained is that there is a disturbance of metabolism in this disease which precedes the attacks, and which ceases with the onset of the actual attack or directly after the attack; and it seems highly probable that this disturbance of metabolism is the cause of the onset of the attacks. Since creatinin is closely related to muscular metabolism, and its excretion shows the peculiar relation that it does to the attacks, and since the disease itself in its main clinical features is one affecting the muscles so prominently, it seems probable also that the essential feature in the disturbance of metabolism that apparently causes the attacks is an alteration in the chemical processes in the muscles themselves. This latter suggestion, however, cannot be considered to be proved.

The manner in which the reduction in creatinin excretion comes about cannot be stated. Mere retention of creatinin cannot be seriously thought of, for the total amount of creatinin excreted through a period including an attack and an interval was in all instances far below the normal. The only explanations for the figures are either reduction in the amount of creatinin produced, transformation of excessive amounts of creatin or creatinin into other substances, or a combination of the latter with retention. Mere reduction in the creatinin production is not an acceptable explanation, since the figures were lower than those that should be furnished by the diet alone if the production of creatin or creatinin in the body had ceased. Hence, whether there was retention or not, it seems most probable that the alteration in metabolism apparently producing the attacks is associated with the transformation of most of the creatin or creatinin into other substances. As to the relation of creatin and creatinin to the symptoms of the disease, I think it may definitely be denied that creatin has anything to do with the production of the paralysis. Pure creatin when ingested, when administered subcutaneously, or when injected directly into muscles, is apparently harmless; and, furthermore, the muscles normally contain large amounts of creatinin. A similar statement as to any paralytic effects is, by most authors, made concerning creatinin; but this statement is based merely upon the results of ingestion or subcutaneous or intravenous administration of creatinin. The two reports which I have been able to find which deal with the direct action of creatinin upon muscles state that when used in this way creatinin produces a brief period of paralysis or profound muscle fatigue, which is followed by entirely normal conditions of the muscles without any permanent effects. So far as I have been able to determine there has been no confirmation of these reports, and they are both old. It is, therefore, impossible to draw any conclusions from them; but a further study of the effects of creatinin upon muscles will perhaps prove of importance in determining the nature of periodic paralysis.

DISCUSSION.

DR. CROFTAN said that he had never seen a case of periodic palsy. He thought that Dr. Edsall's work was brilliant, but that the results were puzzling, and the general urinary findings too isolated to permit of far-reaching speculation. He believed that it was important to do two things in the further study of such cases: First, to make a careful estimation of the creatin in the diet; and, second to estimate not only the total nitrogen, but also the urea. He thought that the creatin excreted might be derived either from the ingesta or from the catabolism of the patient's own muscle tissue. As creatin is one of the chief precursors of urea the estimation of the urea excretion should not have been omitted. If no creatinin is excreted, either no creatin may have been formed or ingested, or else it may all have been converted into urea. He asked Dr. Edsall whether he had obtained a corresponding increase of urea with the diminution of creatinin.

Dr. Edsall, closing the discussion, said that the diet during the periods of especial importance (those preceding the attacks) had been fairly constant—the mixed ward diet of the Orthopedic Hospital. He also said that the creatin of the food had not been estimated, as such a procedure is impracticable, and, further, the amount of urinary creatinin produced by a given quantity of creatin in the food is not at all definitely known. The only satisfactory way of wholly excluding the effects of diet would be to use creatin-free food. He believed, however, that diet could not be thought to have had any marked influence. *November* 14, 1901.

Injuries of the Brain.

WILLIAM S. WADSWORTH, M.D.

To venture on such a well-worked and extensive field would imply great temerity unless one's opportunities for study were exceptional. For the past two years I have been constantly observing and studying cases, each one of which demanded a thorough comprehension of the many intricacies of the problems involved. It is from this rather large experience that I venture to draw certain deductions. I must by way of preparation outline the problems that present themselves and their relations to each other.

Injuries to the brain are seldom simple. We almost always find several injuries, and we are often compelled to estimate the relative values of each in the study of the case; further, we must always be sure that there has not been some source of injury that would escape superficial observation, or one that acted, perhaps, only for a time, or so as to complicate those that are apparent.

Injuries to the brain may arise from

Causes without the body	direct	heat or cold. electricity. mechanical forces.
	(indirect)	
Causes within the body	direct	chemical. mechanical.
	(indirect)	

The study of the indirect methods of causing injury, while necessary for a proper understanding of certain cases, is seldom more than a study of those causes that give rise to some form of direct violence (such as any influence causing increased heart action being the indirect cause of apoplexy). Such study would lead us too far for the present paper. Such causes as fall in the domains of bacteriology and the study of tumors must also be simply indicated rather than discussed. The vast significance of the indirect action of bacteria by means of chemical substances and of secondary infections must always be kept in mind.

Before we can measure the factors of the injury done we must clearly grasp the peculiar properties of each of the possible forces—the times and places of their application and the intensities of the forces applied. If we have the injury, and are required to form a judgment regarding the forces or conditions of application, we must go a step further and have definite standards in our minds regarding the quantity of effect from each given force, with an estimate of the probable value of possible conditions.

Every acting force meets resistance that tends to modify its action. There are certain groups of conditions that modify the action of all injuring forces.

1. Condition of the nervous tissue.
2. Condition of the membranes.
3. Condition of the skull.
4. Condition of the circulation.

These four are to be kept constantly before the mind in all cases, their relative importance being determined in each. Conditions of the nervous tissue include all physical, chemical, and physiologic properties.

(Illustration: A resistant and elastic brain tears less easily; a highly vital brain will resist drugs, as alcohol, or shock more readily than a soft one.)

The conditions of the membranes and skull are confined to such physical properties as texture, distribution of material, and general structure. These depend upon the vital properties.

The conditions of the circulation, so frequently neglected in the study of cases, imply not simply the blood pressure, but also the condition of the blood and of the vessels.

Having in mind the conditions we return to the forces.

1. *Heat.* The effect will depend on the intensity, duration, place of application, and on the power to resist, to transform, and to dissipate the force applied.

(Sunstroke: It is a matter of common observation that persons resist insolation differently. Some perspire, and so diffuse the heat readily; others, by pigment, transform the heat at the surface, so that it does not enter; alcohol and other chemical substances materially affect the resistance.)

2. *Electricity* is a rare cause of injury, but must be mentioned as an occasional cause.

3. *Mechanical Forces.* By far the most common causes. Appear simple, but require for their understanding a working knowledge of mechanics that is not common.

The nature of the material of the instrument that inflicts the injury must be studied in relation to its elasticity and cohesiveness as well as the force and velocity with which it is propelled. (Ex.: sand-bag, fist, stone.) If the instrument is stationary and the brain moves, the problem holds these factors: The size, shape, mass, and momentum, as well as the direction of motion of both instrument and head, are to be estimated in every case. The structural peculiarities of the skull, its contents, and coverings form a special study in each case.

Injuries to the brain from within depend on the (1) condition of the blood, (2) condition of the vessels, (3) condition of the heart.

These conditions act as very important factors in many injuries where the initial forces are applied from without. They often determine the extent of a complex injury, and, where the initial force has simply injured a vessel, may be the direct factors in causing the injury to the brain.

The chemical condition of the blood is of significance from the toxic substances it may contain and from its clotting properties when shed.

(Alcohol stimulates the heart's action, affects the size of the terminal vessels, and directly acts on the brain tissue, besides indirectly adding factors that may have determined the cause of the injury.)

There are certain modifying factors that may be spoken of as pathologic. Normally the heart, through the vessels, causes a continuous massaging of the brain. If the vessels become stiff, tortuous, or otherwise modified, this massage of the brain is interfered with and the brain will not resist so well the direct throb of the unconfined blood of a serious hemorrhage. If the vessels become diseased an injury to them may have an effect on the brain very different from that produced with normal vessels, (aneurysm or arteriosclerosis). If the heart is weak, the resulting hemorrhage is likely to be less. If the heart is hypertrophied or acting with unusual force, we expect greater damage than under normal conditions (apoplexies in uremic conditions). If the vessels become stiff the heart's action tends to rupture the small terminal vessels.

If the brain, by reason of continued action of chemicals, as alcohol or morphin, becomes "wet," then a fracture of the skull becomes more disturbing by draining away the fluid which the abnormal brain has previously rested in.

If certain general conditions, such as give rise to purpuric phenomena, either by vasomotor disturbance or by direct action on the tissues, exist, hemorrhages are apt to be more severe.

If there is increase of intracranial pressure, the effect of an injury may be very considerably affected.

If a true traumatic encephalitis results from the injury, the phenomena of compression may appear where the amount of hemorrhage was insignificant and the other effects apparently very slight.

The mechanical problems offer opportunities for the most careful thinking. A force is applied as a wave or series of waves, and may come in one or more directions. It must be transmitted from the area of application. If through the vessels, as in spontaneous apoplexy, the anatomy of each case alone can explain the mechanism by which the injury was done, because of the variability in the vessels. If from the outside, the transmitting power of the skull must be analyzed.

Probably nowhere in the literature of medicine is bad thinking more evident than in the discussion of mechanical injuries to the brain. The momentum of the moving body, whether it be an instrument or the head, can be judged of with more or less ease by any good mechanic; but the transmission of the force through the skull and brain, with a true comprehension of the foci of primary application and secondary condensation, requires the readiness and penetration that come only after long and careful study of the structural values of different skulls. The understanding of the formation of lines of fracture, of concussion, of contrecoup, all depend on a power to judge of the relative values of the resistance, elasticity, resiliency of the various parts of the skull, and of the value of the structural peculiarities which must modify the blow by concentrating, retarding, diffusing, or deadening the force applied.

Types of skulls, such as thin, thick, brittle, rough, long, short, low, flat, and round, are in a general way well to recognize, but such general observation is wholly inadequate. To note the thin spots in a thick skull; to see a skull that is thin, almost a paper skull, stand a terrific blow, because of great resiliency, while a thick one cracks with a trifling rap, because it is almost as brittle as glass; or to see the jumps a fracture will make, because of bosses of strong bone or sutures; all these are parts of the study of brain injury that cannot be written out, but must be studied from skulls both fresh and dry.

The injuries that may come from mechanical force are:

1. Concussion.
2. Compression.
3. Hemorrhages.
4. Solution of continuity.
5. Any combination of these four.

These are too well known to need further discussion.

A few factors still remain to be mentioned in order to complete the survey. In external causes, protection offered by clothing or other objects—by the hair, scalp, and peculiarities of the portion of the skull. The condition of the bones with relation to the sutures. The possibility of injury transmitted through the lower jaw and spinal column. The transmission of violence through the vessels, either from the body or the neck, causing hemorrhage without marks of violence on the surface.

[Note.—The foregoing is a very much condensed summary of the paper presented. The mechanical principles of transmission and condensation of force were fully illustrated with skulls; also a variety of structural peculiarities.

I wish to record my obligations to Dr. Greenman, of the Wistar Institute, and to Prof. Stone, of the Academy of Natural Sciences, for allowing me to examine the very valuable collections of skulls in their keeping.]

Secondary Carcinoma of the Lung (Hematogenous Infection).

W. M. L. COPLIN, M.D.

(*From the Laboratories of the Jefferson Medical College Hospital.*)

I am indebted to Dr. E. Q. Thornton for the privilege of making an autopsy in this case.

The patient had had scirrhous cancer of the right mamma for at least two years. She had persistently refused operation, and had resorted to numerous quacks without any material alteration in the tumor. There had been but little ulceration, and clinically the tumor was apparently of the type commonly designated atrophic or withering scirrhus. The axillary glandular enlargement was not conspicuous. We were permitted only to examine the thoracic and abdominal cavities; the central nervous system was not examined.

The viscera generally were not macroscopically involved, with the exception of the lungs and a few small nodes in the liver. Neither macroscopically nor microscopically were the other organs cancerous. The pericardium was not cancerous.

The most interest in the case is in the pleura and lungs. The lungs did not recede when the chest was opened. They were a little more dense than usual, but nowhere were they solid or airless. The groundwork of the lung was a little darker in color than the normal lung. There was no edema and no marked congestion. A conspicuous feature both on the pleura and incised surfaces was the presence of grayish nodules varying in size from scarcely perceptible pin-point, dot-like areas to masses 0.5 cm. in diameter. These latter nodules are upon the pleura. They are grayish or pearly white, rising above the pleural surface to a height of 4 mm. or 5 mm. The smaller areas are not elevated, but can be seen through the pleura. The organ is incised with possibly a little more resistance than normal; its cut surface is universally and quite uniformly dotted over with grayish markings similar to those noted as present upon the pleura. The resemblance of these bodies to miliary tubercles is quite striking. None of them show any caseation. At a few points along the interlobular septa there are grayish streaks indicative of linear distribution of a lesion similar to that presented in the nodular areas. There is no evidence of infarction. The lung is not edematous; the pleural cavity had been obliterated by adhesions and the lobes of the organs fused.

We were not permitted to dissect up the axillary vessels, so it is quite impossible to say exactly how the original neoplasm had reached the blood supply.

Histology. The air vesicles are free from any exudate; the larger part of the lung structure presents no important alteration. The conspicuous figures are quite characteristic cancer areas rather of the scirrhous type, neither the cancer cells nor the stroma showing any unusual feature. The carcinomatous infiltration of the organ occupies nearly all anatomic areas. It is inter- and intralobular in the vesicular walls, around the bronchi, along the course of the septa, immediately beneath the pleura, etc.

The second interesting point is the presence within the blood-vessels of numerous cancer emboli. Only occasionally one finds a small vessel actually plugged by cancer; for the most part the cancer cells are found lying free in the blood, and sometimes in one vessel of some size clusters of cancer cells can be recognized. They possess the same tinctorial and morphologic characteristics as the cancer cells recognizable in the lung tissue, and are quite like the cells seen in the original growth. The unusually wide distribution of this process in both lungs and the presence of emboli in the blood clearly establish the hematogenous dissemination of the lesion. *December* 12, 1901.

Abscess (Chronic) of Liver, Recrudescence Due to Secondary Infection (?); Thrombosis of Hepatic Vein and Vena Cava; Extensive Necrosis of Liver; Hemorrhagic Infarction (?).

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AND
L. H. PRINCE, M.D.
(*From the Laboratories of the Jefferson Medical College Hospital.*)

Anatomic Diagnosis. Chronic adhesive peritonitis; purulent peritonitis; chronic abscess of liver; thrombosis of vena cava; acute nephritis. (Only the liver presented.)

M. R., aged fifty years; nativity, Italy; occupation, laborer.

On inspection *in situ* the organ extends 3 cm. below the costal arch, and appears to be slightly enlarged. The organ is lightly adherent to the diaphragm. When these bands are broken down a number of pockets of purulent fluid are disclosed. This fluid was identical in appearance with that found in the peritoneum—*i. e.*, a thick and grayish-colored fluid, in which were varying sized flocculi, of a yellow, somewhat dense material—the abdominal cavity contained 3500 c.c. of this fluid; specific gravity, 1020. On inspection, after removal, a large, slightly elevated, pale area is located on the posterior part of the upper surface. This area is entirely on the right side of the suspensory ligament, and is 10 cm. in diameter. It fluctuates upon palpation. On incision this is found to be a cavity 15 cm. in diameter, containing 300 c.c. of a viscid, pale yellow fluid, which, after standing about thirty minutes, congealed so that inversion of the vessel without loss of contents is possible.

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After careful cleansing the wall is seen to be quite ragged on its inner surface, of a lemon color, somewhat translucent in appearance, and varying from 0.5 cm. to 1.5 cm. thick. The parenchyma of the liver is brownish in color, with a network of yellow traced over the cut surface. The lines of the mesh range from 0.5 mm. to 1 mm. wide over the larger part of the surface; but as the abscess is approached these lines widen and blend with the substance of the wall and partake of the color of the wall.

On severing the hepatic vein a thrombus is incised. This thrombus is found to be continuous with one in the vena cava (inferior), extending from the right auricle to the saphenous and femoral veins of the left extremity. The right branches of the common iliac are less involved. An extensive edema of the left leg was noted.

Section of the radicles of the hepatic vein discloses the presence of a thrombus along these structures, and in a few instances the thrombus reaches the smaller branches. The organ weighs 2100 grams. Specimens were fixed in Beasley's fluid, infiltrated in paraffin, sectioned, and the sections stained in many ways. The pus was examined, stained and unstained; cover-glass spreads and inoculations on various media were also made.

Sections including the wall of the abscess and the adhering contents of the cavity show this contained material to be composed mostly of polynuclear cells, a large amount of cellular detritus, and free and fragmented nuclei. This cellular aggregation and necrotic material is surrounded by a zone of young granulating tissue, in which elastic tissue is quite abundant. All the elements usually found in this type of tissue are readily recognized. This zone fades into a layer of rather dense, wavy, fibrous tissue, rather rich in spindle cells, among which are somewhat circumscribed polynuclear and lymphoid cell accumulations. This zone averages 1 cm. in width. An area of much altered liver structure is now observed surrounding this band of fibrous tissue. The cells of the organ are in an advanced state of necrosis. The outline of the cells is obscure, in many instances even lost, and where any cell resemblance remains the protoplasm of these cells is exceedingly granular. The nuclei present a peculiar granular appearance that is very striking. The areas of necrosis for the most part are located in the so-called arterial or intermediate zone of the lobules, and where the degeneration is most marked the polynuclear cells are conspicuously abundant. A rather large number of double nucleated cells tinctorially resembling liver elements are observed. The least affected of the liver structure is seen to be distributed in small islands around the lesser bile ducts and hepatic central vein, and is seldom more than three to four cells wide. The portal vessels are conspicuous and surrounded by irregular bands of fibrous tissue. These areas are notably infiltrated with lymphoid and a very few polynuclear cells. The columnar cells of the bile ducts are faintly granular.

A study of one of the smaller veins show a thrombus of fibrino-cellular tissue. The wall of the vein containing this thrombus is thickened, extensively fibrous, and contains a large amount of elastic tissue. Organization of the clot is well shown at its periphery, where can be seen the presence of fibrous tissue in rather prominent outline, quite well infiltrated with spindle cells. Other vessels show a remarkable proliferation of the endothelium that extends in plates into the lumen.

The periportal distribution of the liver tissue is quite conspicuous in the sections somewhat removed from the abscess area. The number of layers of cells around the ducts and vesicles is somewhat larger than in sections nearer the abscess.

The necrosis is more readily recognized as being of the coagulation variety, and shows an abundant infiltration with blood cells.

Other sections show the necrosis to extend from the central vein of the lobule. In the necrotic areas the liver cells are destroyed completely, there remaining only threads of connective tissue, forming meshes, which meshes are packed with well-preserved erythrocytes. The central veins do not appear to be at all dilated. It might be said that some of the areas in this part of the specimen appear, at first glance, not unlike the caseous areas of chronic tuberculosis. A coppery-brown granular pigment is observed in some of the liver cells.

A careful search in the pus and abscess wall failed to disclose the presence of any body resembling an ameba.

Bacteriology. The spreads contained an encapsulated diplococcus and a slender bacillus. By plating, cultures of the staphylococcus pyogenes albus and colon bacillus were obtained; the encapsulated coccus, arranged in pairs, and by far the most conspicuous organism in the spreads, was not cultivated. The diplococcus presents the morphology and tinctorial characters of the pneumococcus.

Diagnosis and Remarks. This patient had lived in districts where amebic dysentery occurs, but no history of the affection could be obtained. The intestine was entirely free from lesions. The wall of the abscess clearly indicates that it is old, possessing a fully developed fibrous layer limiting the cavity, and with progressing fibrosis extending at its periphery. We are of the opinion that the lesion has become active as a result of recent infection, as indicated by the bacterial findings, extensive necrosis, peritonitis, and nephritis. The old adhesive peritonitis probably occurred at the time that the abscess was primarily active. The age of the thrombosis and hepatic infarction can be surmised only.

The infarction appears to be more recent than the extensive thrombosis, and particularly the thrombosis of the vena cava, would indicate. We believe that the older part of the thrombus is in the vena cava, and the hepatic thrombi are more recent, probably dating from the last infection. We admit that the extensive necrosis, particularly marked in the left lobe, may have resulted from the infection without coincident infarction, but think that the many plugged veins and the perilobular and intralobular extravasations afford the picture of an infarct. *December* 12, 1901.

Cancer Thrombus in Branch of Hepatic Vein, with Infiltration of Wall.

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AND

L. H. PRINCE, M.D.

(*From the Laboratory of the Jefferson Medical College Hospital.*)

This specimen was observed in a cancer of the liver secondary to cancer of the pylorus. There is nothing unusual in the secondary nodules in the liver, but on incising the organ there was found a large hepatic vein, nearly 0.5 cm. in diameter, upon one wall of which there was noted an elongation nearly 2 cm. in length, thinning off at either end, and possibly 5 mm. in thickness near its center. It extended around the lumen of the vein to a distance of approximately 0.5 cm.

We were curious to know whether it was an involvement of the vein that had extended into the surrounding tissue, or involvement of the vein from the surrounding tissue. The indications all pointed to the latter view.

A small portion of the wall of the vein containing the thrombus was removed, and serial sections were made.

These show that the intima of the vein is no longer recognizable under the thrombus; that the fibrous and elastic layers are involved by the new growth, which rests directly upon the subendothelial tissue. Stains for elastic tissue yielded only negative results.

The thrombus is made up of typical cancer, with an abundant collagenous stroma and small alveoli packed with epithelial cells. Smaller alveoli are to be recognized in the vein wall, although they are not abundant, and around the vein the cancer presents no unusual feature. It is clearly an instance of cancerous involvement of the vein from the adjacent cancer nodule. Serial sections show that the point of nodular invasion of the venous wall is truly small, and that the cancerous thrombus extends as a plate along the axis of the vein almost as far against the blood stream as with it Where the thrombus spreads out over the vein the endothelium of the intima is absent; the surface of the cancer thrombus bears neither clot nor endothelial covering.

December 12, 1901.

Fatty Cirrhosis in the Liver of a Dog.

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AND
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(*From the Laboratories of the Jefferson Medical College Hospital.*)

The specimen is that of a dog's liver, removed from the animal in the anatomical laboratories of the Jefferson Medical College during the special course given in comparative anatomy.

The dog was a mongrel, male cur, brownish in color, well nourished, the muscles normally colored and possessing an abundance of adipose tissue. Death had been brought about by asphyxiation with illuminating gas.

An ascites estimated at between one and two liters was present. Careful examination disclosed no gallstones nor evidence of any other obstructive lesion, past or present. The liver was not adherent to the diaphragm or to any of the surrounding viscera. The organ was firm and resistant upon palpation, and weighed 195 grams.

The liver consists of six lobes (one was removed for histologic study). It possesses a markedly granular, or, possibly better, a "hobnail" surface. The smaller lobes, and particularly the under surfaces of both large and small lobes, present this appearance more conspicuously than the diaphragmatic surfaces. These tuberous projections are on the average of about 3 mm. in diameter and possibly 1 mm. high.

Here and there on the diaphragmatic surface of the superior and larger lobe one observes the presence of nipple-like elevations, each surrounded by a very narrow depression about 1 mm. in depth. The surfaces of these elevations are minutely granular. A few decidedly puckered scar-like depressions are also noted.

The edges of the lobes are sharp, with occasional indentations, varying from 0.5 mm. to 2 mm. in depth.

The ground color originally was a light reddish-brown, with a mottling of yellow and dark-red irregular spots from 1 mm. to 5 mm. in diameter. The yellow spots predominate, and fade almost imperceptibly into the ground color. The red spots were more sharply outlined, and occasionally could be seen merging into the yellow areas. This color picture could be most clearly seen on the freshly cut surface. One could not determine with certainty, macroscopically, the presence of fibrous tissue, although the presence of a number of pale, rather hyaline linear markings seemed to suggest it.

The gall-bladder is observed to be distended and to extend 2 cm. beyond the border of the lobe. The bile is a somewhat copper-colored, slightly viscid fluid. Quantity, 10 c.c.

Specimens were fixed in picrosublimate solution and infiltrated with paraffin. A further number of specimens were treated with Flemming's solution and infiltrated with paraffin and celloidin. Sections were stained with hematoxylin and Van Gieson's mixture, toluidin blue, etc.

Histology. For some reasons not determined by the writers—although the same condition has been observed in other organs from man, and animals killed with coal gas—fixation is imperfect, infiltration difficult, and sections extremely fragile. The organ contains a notable increase of connective tissue distributed in a most irregular manner; in some areas the connective tissue is old; these areas are small and infrequent, but little of the connective tissue having reached that age which fully formed fibrils elect Van Gieson's stain.

The older masses of fibrous tissue are near the portal canals and surround the larger branches of the portal vein and some of the larger bile ducts. Occasionally strands of very fibrillated tissue, electing Van Gieson's stain, can be seen traversing the intralobular areas as finer bands. Such masses, however, are scarce. The fibrous tissue between the lobules is clearly of recent formation. In many areas the cells are still lymphoidal, but for the most part the young connective tissue takes the form of spindle elements, long and short, possessing ovoidal nuclei.

The distribution of the fibrous tissue is also unusual. In some areas groups of lobules are surrounded by bands of fibrous tissue, 1 mm. or 2 mm. in diameter, and occasionally such masses will be quite free from fibrous tissue between the lobules. The condition in such areas is practically that commonly called polylobular cirrhosis. In other areas individual lobules are surrounded (monolobular cirrhosis), and in still other areas the connective tissue can be seen entering the lobules, and sometimes approaching almost to the central vein (intralobular cirrhosis).

The amount of fat in the liver cells is most conspicuous. For the most part the fat is at the periphery of the lobule, although this is by no means a constant phenomenon, as some of the lobules contain centrally placed areas of fat. The fat is best seen in the osmicated preparations, although, unfortunately, Flemming's solution has penetrated but little. The irregularity in location is here admirably shown. The intracellular location of the fat shows nothing unusual. Many of the liver cells not containing fat appear small and shrunken. Around some of the bile ducts there is an increase in the connective tissue, and occasionally this tissue is old, but for the most part comparatively recent. The biliary epithelium shows in many areas desquamative changes. Occasionally it is necrotic and lying free in the bile vessels. In still other biliary ducts granular acidophilic material can be found in their interior. Quite a number show no abnormality.

Diagnosis and Remarks. The condition is clearly one of fatty cirrhosis, with an unusual distribution of the newly-formed connective tissue. The cirrhosis may be said to be in some areas polylobular, in other areas monolobular; and while, for the most part, it is perilobular, it is occasionally intralobular. Evidences of proliferation of the biliary ducts is wanting. Fatty infiltration is conspicuous. It is not possible to give the cause, but the findings indicate that the lesion must be regarded as consecutive to a cholangitis non-suppurative in character.

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Report of Some Experiments on the Formation of Bile Acids and Bile Pigments; A Contribution to Our Knowledge of Icterus.[1]

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(*From the Pepper Clinical Laboratory of the University of Pennsylvania, Woodward Fellowship of Physiological Chemistry.*)

ABSTRACT.

It will be our object to demonstrate in this report:

1. That the bile pigments and the bile acids are not formed by the liver cells.

2. That the bile pigments and the bile acids can be formed from hemoglobin outside of the organism by a purely chemic, fermentative process and without the intervention of the liver cells.

No one has so far seen bile pigments or bile acids within the cells of the liver, excepting in certain pathologic conditions; in judging of the role of the hepatic cells in the formation of these bile constituents the latter finding is without significance, for the reason that secondary imbibition of the liver cells with bile constituents may have occurred. No bile pigment or bile acids can, further, be manufactured from normal liver cells if care is taken that all the bile pigment and all the bile acids that are contained in the channels of the liver are removed; the reported discovery of the bile constituents named in liver cells must be attributed to a faulty technic in this respect on the part of the different experimenters.

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[1] An elaborate report, including all the details of animal experiments, of laboratory technic, etc., will be found in the Philadelphia Medical Journal, January 18, 1902.

Bile pigment is undoubtedly formed from blood pigment, hemoglobin; this is demonstrated by the increase of bile pigment excretion in the bile following the injection of hemoglobin or the administration of certain hemolytic substances; in addition the liver possesses the power of arresting and of excreting any bile pigment that may be present in the circulation. That hemoglobin is converted into bile pigment in the liver seems, therefore, established, and as the liver channels secrete only mucus, the bile acid and bile pigment-forming function, it *appears*, must be relegated to the liver cells.

The bile acids are also probably formed from hemoglobin; as one of them contains a sulphur molecule, we can assume that they are derived, directly or indirectly, from the proteid radicle.

In order to determine, if possible, the exact role of the liver cells in the formation of the bile acids and the bile pigments, the following experiments were undertaken:

Following the example of a number of the pupils of A. Schmidt, a pulp of liver cells was prepared by scraping the surface of sections through fresh livers and the pulp brought in contact with dilute solutions of hemoglobin. I could corroborate the statement made by Anthen that the simple bringing together of liver cells and of hemoglobin is followed by no reaction whatever. In order to simulate as much as possible the conditions actually existing within the liver, it was decided to add a certain proportion of glycogen to the above mixture; if this is done the hemoglobin is, in fact, destroyed, and the fluid over the liver pulp turns from a cherry-red to a pale-yellow. This conversion occurs at room temperature and occupies about five days; at body temperature it occurs more rapidly. At the bottom of the flask a brownish sediment containing traces of bile pigment and in the supernatant fluid a trace of bile acids will be found.

The destruction of hemoglobin, according to the researches of Schwartz, is a property of all living protoplasm; and, as the liver-cell pulp undoubtedly contained traces of the bile pigments and the bile acids, these experiments were hardly available for the purpose of determining anything definite in regard to the role of the liver cells in the production of these substances.

As it is manifestly impossible to obtain liver cells without a slight admixture of bile constituents, we proceeded as follows basing on the hypothesis that possibly the "vital" action of the liver cells had nothing to do with the formation of the bile pigments and the bile acids. I felt justified in entertaining this view from the negative findings chronicled in the experiments with surviving liver cells in the absence of glycogen.

The liver of a calf was divided into several pieces, while still warm, and from the cut surfaces a considerable quantity of bloody pulp was scraped and this pulp rapidly washed with water until the washings were quite clear and bloodless; the bulk of the water was then expressed and the residue placed into absolute alcohol and allowed to remain there for two weeks. It was expected that at the end of this time all "life" in the liver cells would be destroyed. The coagulate was freed from alcohol by washing with ether and the ether allowed to evaporate *in vacuo*. A dry, amorphous mass, consisting of liver cells and strands of connective tissue, remained. In order to completely destroy the integrity of the liver cells, the mass was mixed with sand and powdered; from the brownish powder an extract was made with water. This contained no coagulable albumin.

On evaporation to dryness only a small quantity of dry residue was obtained, consisting largely of inorganic salts and of a small quantity of organic material. The extract contained no bile acids nor bile pigment; the latter had been dissolved in the alcohol and were determinable there.

A small quantity of crystallized hemoglobin was now dissolved in water and 1 per cent. of dextrose added. (Dextrose was employed in the place of glycogen because it was so much more readily procurable and because this substance is as much a specific carbohydrate constituent of the normal liver as glycogen; further, because the above-named authors had found that the destruction of hemoglobin proceeded as well with dextrose as with glycogen.) To 200 c.c. of the mixture of hemoglobin and dextrose 50 c.c.

of the liver-cell extract were added, and in addition a small quantity of thymol to prevent bacterial action; the whole was kept at room temperature for a week.

At the end of this time it was found that all the hemoglobin was destroyed; the fluid had become quite colorless and contained bile acids; the brownish sediment at the bottom of the flask contained a substance that gave the typical reactions of bile pigment. At the same time a portion of the sugar had been destroyed, and the supernatant fluid contained no albumin.

Here, then, a conversion of hemoglobin into bile pigment and bile acids had occurred without any "vital" action on the part of the liver cells. The process was a chemic one. The active agent is a substance that is soluble in water, and is, therefore, unorganized.

It was next attempted to determine, if possible, the source and character of the soluble substance contained in the liver-cell extract. The whole process resembled a true digestion, a fermentative process, so much that it seemed rational to test the fluid for the presence of a ferment with digestive properties.

For this purpose fibrin flakes were placed in the liver-cell extract and the mixture slightly alkalinized with a 1 per cent. solution of soda. A partial digestion of the fibrin occurred at body temperature, and at the end of forty-eight hours albumose, peptone, and some tyrosin were found in the liquid. In an acid medium no digestive destruction of fibrin occurred. If the mixture was first heated to 65° the ferment became inactive and the fibrin remained intact.

These findings made it probable that the active substance in the liver-cell extract was none other than trypsin. This suspicion was strengthened by a comparison of the chemic properties of solutions of the liver extract and of trypsin.

In order to further establish the identity of the two, a dilute solution of trypsin was added to a mixture of dextrose, and hemoglobin solutions prepared as above. At the end of a week this *fluid had become discolored and contained bile acids in solution. The sediment contained bile pigment, and some of the sugar had been destroyed. No albumin was found in the fluid.*

If no sugar was added to the mixture of hemoglobin and trypsin solution the reaction described did not take place, and the ordinary products of an incomplete tryptic digestion were found. No bile pigment and no bile acids were discovered.

A pretty demonstration of these differences can be made *ad oculos* as follows:

Three cylinders are prepared. The first contains hemoglobin solution, 1 per cent. dextrose, and a measured quantity of a dilute trypsin solution; the second the same amount of hemoglobin and trypsin, but no dextrose; the third hemoglobin solution alone. All three cylinders are colored exactly alike, viz., a deep cherry-red. At the end of a week the first cylinder will contain a colorless solution and a brown precipitate; the second one a brownish smear; the third will be unchanged—*i. e.*, red. In this experiment the action of bacteria is not excluded, and sometimes a growth will be found on top of the fluid in all three cylinders. Hemoglobin is, however, very resistant to the action of bacteria, and the fact that the color of the third cylinder remains unchanged is the best proof that bacterial action has nothing whatever to do with the changes observed in the first cylinder. In addition, of course, all necessary precautions were taken in the different experiments chronicled in this report to avoid contamination by bacteria or other micro-organisms.

The unorganized substance, therefore, that can cause the conversion of blood pigment into bile pigment and bile acids in the liver is none other than trypsin.[1]

The question arises, how does trypsin get into the liver? That the liver should form trypsin is, of course, absurd; trypsin must reach the liver from the pancreas. There are two possibilities, viz., it can either leave the pancreas by way of the pancreatic duct and then be absorbed from the intestine, or it can leave the pancreas, possibly in the form of its "zymogen" (?), by way of the pancreatic veins or lymphatics. In the former instance it can only reach the liver in the portal vein; in the latter either *via* the pancreatic veins, in the portal vein, or *via* the lymphatics, the thoracic duct, the jugular, and the heart in the hepatic artery.

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[1] In view of the undefined chemic and physic characteristics of the ferments, we can identify them only from their manifestations—*i. e.*, from their action on stated substances under stated conditions. If, therefore, in the case of two "ferments," all manifestations under equal conditions are found to be equal, we are justified, *faute de mieux*, in considering the two identical.

A number of experiments published elsewhere make it probable that trypsin is in part normally absorbed from the intestine, but that the greater portion reaches the liver *via* the pancreatic veins in the portal blood, or *via* the lymphatics in the hepatic artery; in other words, that the "internal" secretion of the pancreas plays a greater role in the process of intracellular digestion that we are discussing than the external secretion.

Different investigators (Grützner, Hoffmann, and others) have discovered trypsin in a number of organs besides the liver, viz., the spleen and the muscles, but not the kidneys. I have found it in the liver, the spleen, and the muscles, and, in a paper to be shortly published, have shown that a ferment is normally present in the blood that is identical with trypsin, or, at least, not distinguishable from it by known methods. I have also shown that this ferment is carried by the leukocytes, and that it is capable of converting hemoglobin into bile acids and bile pigment in the presence of dextrose. It seems probable, therefore, that trypsin is constantly secreted by the pancreas; that during digestion the greater proportion is excreted *via* the pancreatic duct to perform its important proteolytic, lipolytic, and amyolytic function in the intestine, and that during the periods of intestinal inactivity a considerable proportion is secreted internally, and is poured into the blood or lymph stream to perform an equally important function in intracellular digestion, viz., proteolysis and glycolysis.

All the trypsin that leaves the pancreas *via* the pancreatic veins must reach the liver in the portal vein. A great part is arrested there like many other poisons that travel that path. In the liver the labyrinth of capillary channels, through which ooze sluggish currents of blood, and lymph, and bile, must favor the retention, for a time, of trypsin. That this is not a specific property of the liver can be demonstrated by injecting trypsin solutions into the jugular vein of an animal. The bulk of the trypsin will then be found in the lungs—*i. e.*, the first organ with an intricate system of capillaries reached. From the liver the ferment is carried into the blood current, and, as it is very toxic, is not allowed to circulate free in the serum, but is gathered up by the phagocytes, we must assume, which, harboring it safely in their interior, bear it in a harmless form through the blood stream to its ultimate destination. It is not excluded that the leukocytes gather up some of the trypsin in the lymph- or bloodvessels that leave the pancreas.

When we study the peculiar anatomic arrangement of the arterial, venous, lymphatic, and biliary channels that honeycomb the liver; when we remember that these passages over wide areas are separated from one another by a single layer of hepatic cells only; when we consider, finally, the manifold sources of the fluids that flow through this meshwork we can well understand why (by osmosis and diffusion) an intimate mixture of their different ingredients occurs, and why, as a result, so many metabolic processes occur in the liver. It is ordinarily believed that all the processes of assimilation and of dissimilation that take place in the liver are dependent on some specific, *vital* function of the hepatic cells. This has never been experimentally demonstrated.

In the liver we always have a medium containing glycogen, and by conversion (or prior to conversion) dextrose. For the formation of the bile acids and the bile pigments this is the *first* condition. The *second* one is given in the presence of trypsin that we have discussed. The *third* is given in the constant presence of free hemoglobin; it is derived chiefly from red blood-corpuscles that perish in great numbers in the liver, "the grave of the red blood-corpuscle." (Nicolaides showed that there are from one to two million less red blood-corpuscles in the blood of the hepatic vein than in that of the hepatic artery.) In addition free hemoglobin is carried to the liver in the splenic vein, which always contains some of the hemoglobin derived from the red blood-corpuscles that are destroyed in the spleen. Finally, the leukocytes are known to carry fragments of red blood-corpuscles to the liver, and consequently also bring hemoglobin (Loew, Naunyn, Minkowski). In the liver, therefore, we have an intimate mixture of the three products, and consequently the formation of bile acids and bile pigment. No specific liver function is required. The role of the organ is that of a "mixer," of an "abdominal lung."

If the formation of bile acids and bile pigment from hemoglobin by the action of trypsin in the presence of dextrose is a purely chemic process and altogether independent of the specific action of any particular group of cells, we must conclude that *wherever in the body free hemoglobin is present, together with dextrose and* *trypsin, this conversion into bile products can occur;* in other words, that the formation of bile acids and bile pigment need not occur in the liver alone.

Red blood-corpuscles are constantly destroyed in different parts of the body, and consequently hemoglobin is constantly liberated. Dextrose is universally present, and, as we have seen, trypsin, in small quantities, can be found in many organs, and is present in the leukocytes that can carry it everywhere. Here, then, a trinity of conditions is given for the formation of bile products in almost any part of the body, and the burden of proof is imposed on us, not to show why bile pigment and bile acids are formed in the liver, but to show why they should not be formed elsewhere.

December 12, 1901.

Compression of the Brain in a Case of Hyperostosis Cranii.

WILLIAM G. SPILLER, M.D.

This case occurred in the practice of Dr. James M. Brown. I. am unable to give the clinical history. The patient was a woman well advanced in years. She was said to fall occasionally, and when she did so her head struck the ground with much force. The brain was removed by me, and permission was not given for examination of other parts. The skull seemed to be the only bony structure affected.

The enlargement of the skull was chiefly in the posterior portion behind the ears, though the forehead was also unusually broad. The circumference of the head immediately above the ears was 60½ cm. The line of measurement above the ears passed directly through the middle of the palpebral fissures. Across the skull from the top of one ear to the other measured 32 cm.

The dura was unusually adherent to the calvarium, and, therefore, the brain was removed with the calvarium. After removal of the calvarium and the brain together the adhesions were easily ruptured. The convolutions were flattened and the sulci more shallow than normal. The cerebellum was very much flattened from above downward. The fluid within the ventricles was not increased.

The skull at its thickest portion posteriorly and anteriorly measured 2 cm.; and in its lateral portions measured 1 cm. on the left side, and 1½ cm. on the right side just above the ear.

December 12, 1901.

A Case of Microcephaly.

WILLIAM G. SPILLER, M.D.

In 1897 I made some notes on the condition of the boy W. M., a microcephalic idiot. He was born October 5, 1889. The muscles were well developed; the knee-jerks were prompt, but not much exaggerated; sensation for pain was normal; the reflexes in the upper limbs could not be obtained; hearing appeared to be good, inasmuch as the child turned his head toward a noise or when his name was called. He could not walk, and when stood on his feet he did not attempt to move his lower limbs, although he could stand when the upper limbs were supported. The circumference of the head was fifteen and three-quarter inches, the measurement across the skull from the upper portion of one ear to the other was nine and a half inches, and from glabella to the external occipital protuberance ten inches.

The boy died March 18, 1901, and the necropsy was made by me March 20th. His weight was 20.7 kilograms; his height 121.3 cm. The feet were in the position of talipes equinus, and could not be bent backward fully to a right angle with the legs. The hair on the scalp was coarse and thick. The dura was slightly adherent to the pia over the whole of the cerebral hemispheres, and in some places to the calvarium, so that the latter was removed with great difficulty. The calvarium was thin, and measured at its cut portion one-eighth of an inch in thickness. The brain was not especially edematous and weighed 585 grams. The cerebral hemispheres were of equal size; they did not cover the cerebellum but left about 2½ cm. of each cerebellar lobe exposed. The cerebellum was much better developed than the cerebrum. Each cerebral hemisphere measured, anteroposteriorly, 12½ cm. The fissure of Rolando on each side was nearly perpendicular. The cerebral convolutions were very imperfectly developed, especially in the parietal lobes. The cerebellum measured transversely 10½ cm. The occipital lobes diverged from one another, leaving the superior vermis exposed. The cranial nerves were normal and the pons was well developed. The spinal cord was about as large as it usually is in a child the size of W. M.

December 12, 1901.

Internal Hemorrhagic Pachymeningitis.

WILLIAM G. SPILLER, M.D.

S. T., aged seventy-three years, was admitted to the nervous wards of the Philadelphia Hospital, in my service, August 23, 1901. He had right hemiplegia, incontinence of urine and feces, slow speech, and impaired memory. He talked very little, did not answer questions very intelligently, and it was difficult to understand what he said. His memory for recent events was poor. He did not know how long he had been sick, who had brought him to the hospital, how he had come to the hospital, or how long he had been there. Sensation to pin-prick seemed to be preserved, as when stuck with the point of a pin in the paretic limbs his face expressed discomfort. He could move the right lower limb, but with difficulty, and could not move the right upper limb. The left limbs he could move freely. No muscular atrophy was present. When stood on his feet he rested his weight on his left lower limb, and when made to take one or two steps he dragged his right lower limb. Both knee-jerks were present, but not exaggerated. The Achilles jerk was present on each side, but difficult to obtain. The Babinski reflex was not present on either side, and the movement of the toes, including the big toe, on the right side was that of flexion when the sole of the foot was irritated. The absence of the Babinski reflex on the hemiplegic side was important, as the central motor tract innervating the hemiplegic side was not degenerated, but the motor area of the left cerebral cortex was compressed. The right biceps jerk was prompt, but the right triceps jerk was not obtained.

The patient gradually became more stuporous, granular casts and albumin were found in the urine, and he died with edema of the lungs, September 14, 1901.

The necropsy was performed by Dr. Kalteyer. I shall refer merely to the condition of the brain. A large hemorrhagic cyst, measuring 15 cm. in the anteroposterior diameter and 10 cm. in width about its middle portion, was found on the left inner surface of the cerebral dura. The brain was much compressed by this cyst, the motor area of the left cortex being implicated. Secondary degeneration, even when the method of Marchi was employed, was not distinct, as only a few black dots were found by this method in the right crossed pyramidal tract. The right hemiplegia was caused by pressure. *December* 12, 1901.

Melanosis of the Cerebrospinal Meninges.

D. J. McCARTHY, M.D.,
AND
MAZYCK P. RAVENEL, M.D.

(*From the William Pepper Laboratory of Clinical Medicine and the Laboratory of the State Live-stock Sanitary Board of Pennsylvania.*)

We wish to present in this paper some remarks on the subject of excessive deposition of melanin pigments in the cerebral and spinal meninges, based on a careful study of two cases, one a cow in which the pigmentation was extreme, and the other a human being, in which the pigmentation was not so intense.

CASE I.—The brain and upper portion of the spinal cord of a cow supposed to have died of rabies was sent to the Laboratory of the State Live-stock Sanitary Board for the purpose of obtaining a diagnosis. The clinical history was strongly suggestive of rabies following the bite of a dog, and, as the physician who made the postmortem examination wounded his hand while removing the brain, a positive diagnosis was important. The clinical diagnosis was confirmed by examination of the intervertebral ganglia, of which more will be said later, and also by the subdural inoculation of rabbits.

On macroscopic examination the brain and spinal cord were found to be almost black, the color being most intense over the spinal cord, and gradually fading as the vertex of the brain was reached. It was, however, very distinct over the parietal region, and to a lesser degree over the temporosphenoidal and occipital regions of the brain. The inner surface of the dura, the arachnoid, and the pia were all involved in the pigmentation. There was, perhaps, more pigment in the pia than in the arachnoid or dura, though there was but little difference in the degree of color produced. On cross section of the cord or brain substance, it appeared as if there was an infiltration of the pigment into these tissues. The velum interpositum and choroid plexus of the fourth ventricle were deeply pigmented.

In making the microscopic examination of this case, sections of the cord with the membranes intact were cut and examined, both stained and unstained. Pieces of the pia and arachnoid were also separated from the brain and cord, spread out on a slide and mounted in glycerin without staining. Other portions were stained with hematoxylin and eosin or carmine, and mounted in the usual manner. The relative deposits of pigment were best seen in the unstained sections. The cellular structure and the relation of the pigment areas to the bloodvessels were best studied in the stained preparations.

The pigment was found (*a*) in amorphous masses in irregular-shaped cells surrounding the vessels, and to a lesser degree at a distance from them; and (*b*) as a very granular matter scattered uniformly throughout the tissues and filling up the endothelial cells of the membranes. The cells of irregular conformation were completely outlined by the pigment even in the unstained sections. In some of these cells where the pigmentation was less intense it was found that the coloration was produced by a very close massing of fine granules similar to those observed in the endothelial cells. The relation of these deeply pigmented cells to the pial vessels gave the very striking effect in the unstained sections of bloodvessels with black walls. The examination of the velum interpositum and choroid plexus gave practically the same result as observed in the pia, just described. In the sections in which the spinal cord and its membranes can be studied together a deep brownish pigmentation can be followed deep into the cord along the course of the bloodvessels. The pigment appears to be deposited in the cells of vessel walls. Not only in these cells, but also in the pia, the pigmentation of the connective tissue cells is very intense in the cell body, but the nucleus is left free. In some cases, however, the nucleus is not visible.

Microchemic reactions for iron were tried, but with negative results. As there was a possibility that this pigmentation might have been the remains of an old hemorrhagic extravasation, the negative reactions to the free iron tests left little doubt as to the nature of the pigment. Melanin in very small amounts is found in the pia of the cervical region of the spinal cord in human beings, and in somewhat larger quantity in the lower animals. It is very probable, therefore, that the intense pigmentation in this case was merely an accentuation of the slight pigmentation usually found in the cervical pia, in general so slight as to be inappreciable to the naked eye, though in this animal so markedly increased as to give a black color to almost the entire central nervous system. The only other change discovered in this specimen was a considerable thickening in the walls of the spinal vessels. We were, however, unable to trace any connection between this endarteritis and the pigmentation of the membranes. We were also unable to determine the cause of the arterial disease. The diagnosis of hydrophobia was confirmed by the perivascular round-cell infiltration, the pericellular infiltration, and the capillary hemorrhages in the medulla, and also by the changes found in the ganglion cells of the intervertebral ganglia. These consisted of advanced degeneration and marked vacuolation, with abundant proliferation of the endothelial cells of the capsule, as described by Van Gehuchten and Nelis. We have never met with a case in which vacuolation of the ganglion cells was more marked.

The pigmentation was of long standing, and, of course, had nothing to do with the acute rabic process. In a series of more than sixty cases of rabies in various animals, this is the only one showing a melanosis of a degree sufficient to make it appreciable to the naked eye.

Case II.—The second case we wish to record is that of a deaf-mute who died from tuberculosis. At the autopsy, in addition to an atrophic process affecting the left side of the brain in the occipital and parietal regions, there was a considerable degree of pigmentation of the pia and arachnoid over the pons and medulla, giving to this part of the brain a distinctly darker hue than the rest, but nowhere was it so intense as in the case above described. The microscopic examination gave practically the same results as in the first case, with the exception that the pigment, instead of appearing black by transmitted light, took a reddish-brown hue. The pigment was composed of the same fine granules, but they were fewer in number and not so densely aggravated in the cells. The pigment-bearing cells were not so closely arranged about the vessels as in the first case.

Both these cases are examples of excessive deposit of pigment in tissues in which it is found normally in small amounts. In neither of them had the pigmentation any relation to the pathologic process causing the death of the individual. In the cow the peculiar arrangement of the pigment cells about the walls of the vessels, and the presence of pigment in the walls of the vessels within the spinal cord would support the teaching of Krukenberg that the melanotic pigments are derived from the oxyhemoglobin of the blood by the action of light and the alkaline reaction of living tissues. In a peculiar pigmentation of nerve cells observed in a rabbit poisoned by rattlesnake venom, reported by one of us,[1] after a careful study of the subject we arrived at the conclusion that it was due to the metabolic action of the tissues on the hemoglobin of the degenerated blood. In neither of these cases had the action of light anything to do with the result. We can therefore agree with Krukenberg[2] in so far that the pigmentation was the result of the metabolic action of the tissues on the hemoglobin pigments. After blood extravasation into different tissues there is found a brownish or black pigment giving a negative reaction for iron, and spoken of as melanin, due to the same cause. It is very probable that there are several different pigments of varying chemical composition described under the general name of melanin. Some of the melanotic pigments found in pathologic tissues, such as the melanosarcomas, will give distinct iron reaction (Nencki,[3] Lieber, Abel,[4] Dands, Schmiedeberg,[5] etc.). Schmiedeberg finds besides this iron reaction a varying percentage of sulphur and nitrogen depending upon different stages of albumin degeneration.

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Latent Diffuse Gangrene of the Lungs, with Rupture and Fetid Pleurisy.

JAMES M. ANDERS, M.D.,
AND
JOSEPH MCFARLAND, M.D.

The following case of gangrene of the lung is of interest because of the rarity of the condition and its absolute latency:

John M., aged sixty-nine years, German, widower, shoemaker, was admitted to the Medico-Chirurgical Hospital, October 18, 1901. The patient did not recollect having been ill prior to the present time. For many years he was addicted to excessive indulgence in alcoholics, especially beer. Since about two years ago he has been drinking moderately only.

The present illness dates from October 15, 1901, when the patient was seized during the night with severe stabbing pains in the right mammary region, followed later by cough and expectoration. The sputum had a light rusty color. On October 16th a physician was called, but did not prescribe, and two days later, October 18th, the patient was sent to the hospital. The symptoms and course after admission were those commonly observed in senile pneumonia. The temperature ranged between 99° and $101\frac{3}{5}$° F., with considerable oscillations; the pulse-respiration ratio was much disturbed and the physical signs were those of consolidation of the lower lobe of the right lung. These symptoms and physical signs continued up to within one day of death, which occurred October 21st. Shortly before death took place edema of the previously uninvolved portion of the lungs was shown by the presence of liquid, bubbling rales, but owing to the extreme debility of the patient no attempt has been made to examine the lungs carefully.

At no time during the patient's illness was the slightest fetor, either of the breath or of the sputum, observed. Neither was the expectoration in any way characteristic—*i. e.*, it did not show any tendency to the formation of layers on standing, did not contain fragments of lung tissue, and, as previously stated, failed to emit the customary horrible fetor.

Autopsy. Body of a somewhat emaciated old man. Cadaver in good condition. Rigor mortis moderate; livores mortis moderate. No external lesions or signs of disease.

Thorax. The pericardium was normal. *Heart.* The heart was normal in size; there were milk spots upon the left and right auricles. The chambers contained yellow clots with "currant jelly" adhering to them. From the vessels coagula ½ m. in length could be withdrawn. The muscular substance of the heart was fair, though flabby. The mitral and tricuspid valves were normal. The pulmonary valve also normal. The aortic valves were calcified at their bases, the aorta was calcareous and sclerotic at the heart and at the arch. The anterior coronary artery was like a "pipe-stem" for about 1½ cm. over the middle of the ventricle.

The left lung was everywhere adherent to the chest wall by old adhesions. The pulmonary tissue itself was somewhat edematous and congested. It was somewhat leathery in consistence.

Right lung also adherent to the chest wall and removed with great difficulty. In tearing it away from the ribs the fingers suddenly entered irregular spaces filled with a greenish-brown, fetid fluid, of which probably a liter was removed. This condition constituted a *true fetid loculated pleurisy.* The lung tissue beneath was gangrenous, the entire lower lobe being involved in a diffuse gangrenous process. The tissue was greenish-black in color, pulpy in consistency, stinking and disgusting in quality. The upper lobes were in an extreme degree of edema, so that when incised clear watery fluid ran out. Over the gangrenous area there were blebs from which gas escaped under pressure when incised, evidently resulting from decomposition. The bronchial glands were full of mineral matter—coal-dust—some of the fragments being of good size.

Spleen. Somewhat larger than normal. Substance irregularly mottled, with congested and anemic areas.

Adrenals. Normal; that of the right having a pultaceous medulla which broke down and transformed the organ into a sac when pressed.

Kidneys. Normal in size and shape. Smooth on surface. Capsule stripped well. Substance firm. Probably some parenchymatous degeneration, but nothing apparent to the naked eye. Pelves and ureters normal.

Bladder, normal. *Prostate*, normal. *Liver*, normal; biliary ducts normal and unobstructed. *Pancreas*, normal. *Intestine.* The intestine was not opened. There were no external signs of disease, and the patient had had no symptoms of any intestinal trouble during life.

Stomach. Showed on the external surface, anteriorly over the lesser curvature, a white spot 1½ by ¾ cm. It was less apparent on the mucous surface. It was supposed to be an old scar, though its nature is uncertain. *Esophagus*, normal.

Larynx. Mucous membrane thickened, as from chronic inflammation, with what appeared to be cicatrices above the false cords, especially on the right side. *Trachea.* Red and inflamed in appearance.

REMARKS. In view of the postmortem findings it is obvious that a careful physical examination of the right lung during the last day of the patient's illness might have revealed the presence of pleural effusion, though the loculated condition depending upon the extensive pleuritic adhesions makes it doubtful. On the other hand, the signs indicative of the actual condition were not in evidence thirty-six hours prior to death, when a physical examination was made, and the patient was doing well. Doubtless the gangrene, which succeeded the pneumonia, caused perforation of the pulmonary pleura. The absence of all characteristic symptoms of pulmonary gangrene can be explained by assuming that there was no fistulous communication with a bronchus. But this state of things could probably not have existed for any considerable length of time, and the gangrene probably developed as a terminal condition. This conclusion is also borne out by the symptoms and course of the affection up to within thirty-six hours of death.

The literature contains but few cases of latent gangrene of the lungs—*i. e.*, gangrene without characteristic symptoms.

Vargas[1] reports a case of diffuse latent pulmonary gangrene in a child of three years. In this case there were signs of a massive consolidation of the lung, with flat percussion note and absence of breath-sounds. The putrid odor, fetid expectoration, etc., were absent, as in the case we report. At the necropsy [illegible] lung was found to be in an eaten-out condition [illegible] sue projecting in regular ridges, one above anoth[illegible] case, unlike our own in this respect, the grave [illegible] did not agree with that of an ordinary pneu[illegible]ty-six hours prior to the fatal termination. Ja[illegible] that the lesion probably originated in an infar[illegible] case it is highly improbable that life would have [illegible]ed so long after the occurrence of embolic infarctio[illegible]ranch of the pulmonary artery that supplies the entire low[illegible]e of the right lung.

Rhymer[2] records three cases of diffuse pulmonary gangrene following influenzal pneumonia. In two of them fetid expectoration and marked fetor of breath betrayed the presence of the gangrenous process; while in the third, a case of cortical pneumonia, rupture into the pleural sac was followed by pyopneumothorax, which evinced the nature of the disease. According to Rhymer, the sudden development of pyopneumothorax in the pneumonia of influenza is conclusive evidence of pulmonary gangrene as a secondary event.

Riesman[3] gives brief notes of a fatal case of pneumonia in which the left lung showed a gangrenous cavity, 10 x 10 cm., containing a dark fluid; the left pleura was covered with a fibrinous exudate. During life the exhaled breath emitted a foul odor, but the sputum did not have the character of that of the pulmonary gangrene.

Instances of latent diffuse pulmonary gangrene are extremely rare, very few cases seeming to be contained in the literature. Diagnosis of the condition may be easily possible and justifiable when pneumothorax develops with unusual rapidity in the course of a primary pneumonia.

Latent circumscribed gangrene of the lung is far more common. One[4] of us met with a case of this sort associated with an aspiration bronchopneumonia that ended in recovery, and one[5] of us also observed a case that developed secondary to carcinoma of the esophagus, the softened necrotic tissue of the neoplasm having been inhaled through an opening in the posterior part of the right bronchus, setting up gangrene.

B. F. Wells[6] records a case occurring in a boy who had suffered a traumatic injury (contusion) of the chest. At no time was there any fetor of the breath or any fetid expectoration. In this case pulmonary gangrene was associated with empyema.

Annan[7] observed a diffuse or multiple circumscribed gangrene of the lungs in a girl aged nineteen years. Neither cough, fetor of the breath, nor fetid expectoration had been present. The gangrene was found to be associated with wide-spread pneumonia.

L. E. Holt[8] reports the case of a child, aged three years, in which there was no fetor to the breath and no expectoration. At the autopsy about two-thirds of the substance of the right lung showed multiple gangrenous areas, varying in size from a walnut to a pea. Many of these patches touched each other to form irregular masses; there was no distinct line of separation between the dead and living tissues, however, as in true circumscribed gangrene of the lung.

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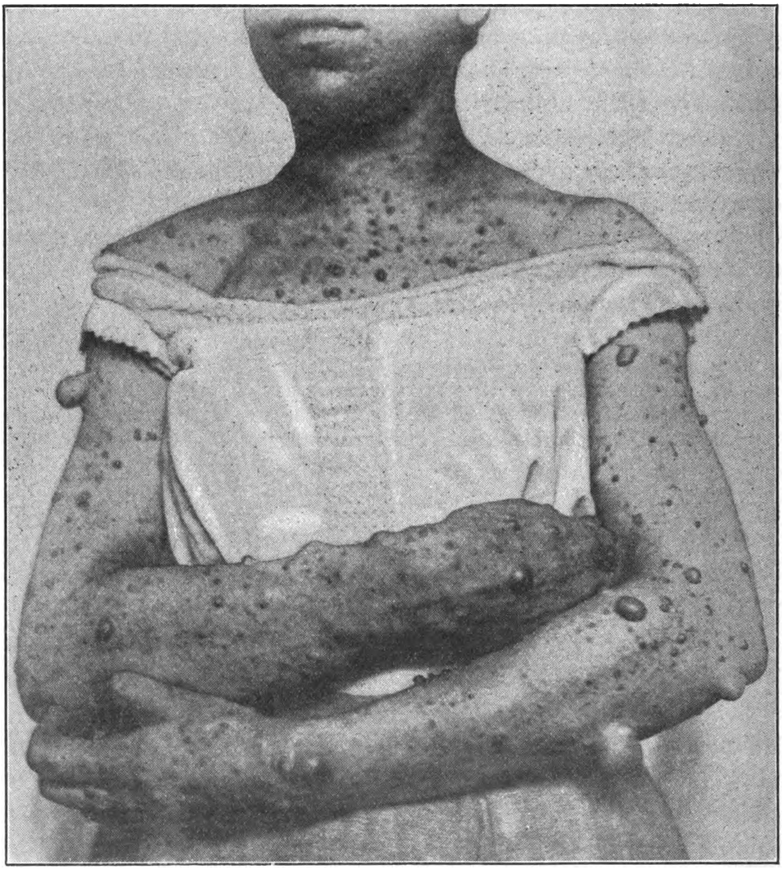
December 19, 1901.

A Case of Fibroma Molluscum.

M. B. HARTZELL, M.D.

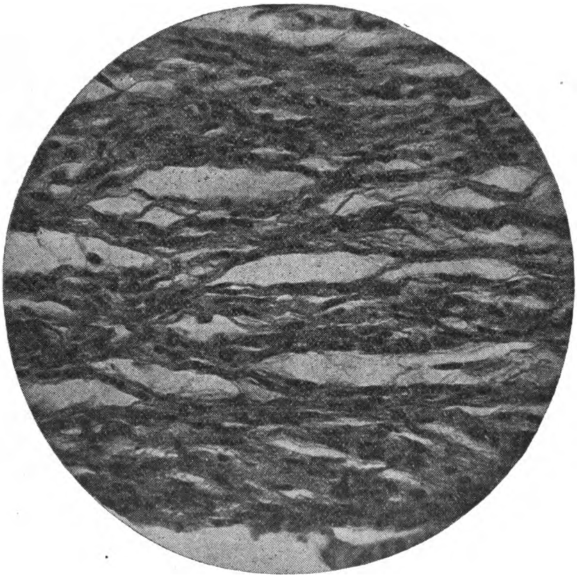
In July of this year G. J., a young unmarried woman, twenty-six years of age, came to the Skin Dispensary of the University Hospital for advice concerning a disease of the skin which was characterized by the presence of great numbers of variously sized tumors distributed over the entire cutaneous surface. These tumors varied in size from a hempseed to a pigeon's egg, the small and medium-sized ones being hemispheric and sessile, while the largest were pear-shaped and attached by a pedicle. They were covered by skin of normal color, soft and inelastic to the touch, the largest growths feeling like empty sacs. They began to appear in early childhood, other members of the family being quite certain that none were present at birth, and increased rapidly in number up until the present time. The general health was unaffected. The patient was a well-developed woman physically, but was evidently somewhat defective mentally.

FIG. 1.



A split-pea-sized tumor was excised from the back for microscopic examination. Sections of this tumor showed that the epidermis was normal, except that the interpapillary prolongations of the rete mucosum had disappeared almost completely owing to the flattening out of the papillary layer of the corium. The body of the growth was formed of fibrous tissue, which, at the periphery, was arranged in a loose meshwork, while in the center it was much more compact. There were many oval and spindle-shaped, deeply-stained nuclei, which were decidedly larger at the periphery of the tumor than in the center. In appropriately stained sections a considerable number of "mastzellen" could be seen. A few apparently normal hair-follicles and sebaceous glands were present, together with a considerable number of small blood-vessels.

FIG. 2.



While there is a general agreement among pathologists as to the anatomic structure of fibroma, there is considerable diversity of opinion as to the part of the skin in which it takes its origin. The deep part of the corium, the connective-tissue wall of the hair-follicle, the connective-tissue framework of the fat lobules, and the fibrous sheath of the nerves have all been described as the place of origin of the tumors. It seems quite probable that each of these structures may be the point from which the fibrous hyperplasia starts, and that in certain cases several or all of them may be involved at the same time.

The etiology of this very curious condition is extremely obscure, but heredity seems to play a part in its production, since it has been observed to occur in several members of the same family and in successive generations. It is worth noting that, as Hebra has pointed out, the subjects of fibroma molluscum are usually poorly developed, physically and mentally, although there are many exceptions to this rule. *November* 14, 1901.

A Case of Spontaneous Rupture of the Heart.

ROLAND G. CURTIN, M.D.

My reason for bringing this specimen before you is to illustrate a condition that might be produced by a weakening of the ventricular walls by disease, such as is shown in the case of myomalacia of the left ventricle, which I have just reported to you. The specimen was presented to me by Dr. J. S. Baer, of Camden, N. J. He obtained it from a patient whom he had under his care. The history was as follows:

Mrs. ——, aged sixty-five years. She had typhoid fever some thirty years ago; otherwise she had always been well, except for periodic attacks of severe pain in the hepatic region.

When first called to see the woman she was up and about the house, attending to her domestic duties. She was moderately jaundiced, with a temperature of 102° F., and complaining of severe pain and soreness in the region of the liver.

The doctor ordered her to bed at once, and placed her under appropriate treatment. In about a week she was free from pain, and the jaundice was much less. Having had no fever for several days, she was considered convalescent. Contrary to instructions, however, she arose, walked about the house, and sat before an open window for some time. It was cold November weather. The next morning the doctor was sent for, and found her somewhat cyanosed, with rapid respiration and pulse, severe pain in the left axillary region, and slight cough. These symptoms continued for five days, when he was again sent for in haste, and found the woman in a state of collapse, with no radial pulse. A faint heart-beat could be heard over the left breast. The face was pinched, cold, and deeply cyanosed. There had been no nausea, vomiting, or straining, but dyspnea was very marked. The patient was very restless and delirious, and complained of feeling smothered. The above symptoms of collapse came on suddenly while the patient was in bed; but, in spite of their severity, she lived for more than twenty-four hours before death occurred.

The postmortem record shows that upon opening the abdominal cavity the gall-bladder was found to contain 125 small gall-stones, nearly equal in size. Both pleural cavities contained large quantities of serous fluid. Hepatization of the lower lobe of the left lung was present. The vessels of the pericardium were injected. Upon opening the pericardial sac it was found to contain a good deal of dark fluid blood. Upon turning up the heart the left ventricle was found to be ruptured to the extent of from 2.5 to 3.75 cm. This rent was closed by a dark blood-clot.

This, then, is the history of the case, and in it we notice several interesting and unusual points:

1. The woman was but sixty-five years old, which is rather young for an accident of this character. When we discuss the causes, it will be seen why a more advanced age than this would render the occurrence more likely.

2. Apparently she was asleep when the rupture occurred.

3. A period of over twenty-four hours elapsed between the time when the rupture presumably took place and the time of death. There is, I believe, a case recorded in which the symptoms came on eleven days before death; but that is a very unusual case, and is cited in all the books as being remarkable. The reason that this patient lived so long is probably because the rupture was small, and also because she was in a quiescent state; only a small quantity of blood was, therefore, allowed to escape slowly, and clot-formation was thereby induced.

The autopsy notes say that this rupture was from 2.5 to 3.75 cm. long. It is now only about 2 cm. long on the outside, and inside it is much smaller than externally, but still large enough to admit the end of my finger. The shrinkage is probably due to the action of the preserving fluid used. The position of the rupture is on the posterior aspect of the outer wall of the left ventricle, which, as statistics show, is the most frequent seat of its occurrence. In Barth's series of twenty-four cases, every one occurred in the left ventricle. Meyer's table of thirty-six cases, all of which are recorded since 1870, shows that twenty-five were of the left ventricle, seven of the right ventricle, and four of the right auricle.

Rupture of the heart is, as must be readily appreciated, a rare condition; and yet, in talking to Dr. William S. Wadsworth, one of the Coroner's physicians in Philadelphia, I asked him whether, in his work, he had discovered any cases, and he said that last year he saw three in six months. He denied, however, that the records of the Coroner's office would indicate that the condition is so common, and admitted that he had seen no other cases since he had been serving in his present capacity.

The causes of rupture of the heart may be stated in a few words: Fibroid and fatty degeneration are the most common. These changes cause the muscle-fibers to become tender, so that they may at any time give way under strain. Another not uncommon cause is occlusion of the coronary arteries, cutting off the blood-supply and interfering with the nutrition of the myocardium. In this way, too, the tissues are weakened, and rupture may be easily produced. Small abscesses occurring in the muscular structure may act in the same way.

It is exceedingly rare to have a rupture of the heart occur in a person that is not exercising or straining. Generally, a person engaged in some usual or unusual muscular effort will suddenly fall and immediately die; but, as we have seen, the rupture may occur some days before death takes place. In such cases a positive diagnosis, although suspected, cannot be made; for, without an autopsy, it is not justifiable to say that the symptoms which might be produced by other well-known conditions were, in a given case, caused by rupture.

In the spring of 1899 Dr. Newton, of Montclair, N. J., presented a specimen at a meeting of the American Climatological Association held in New York City. It was taken from the body of a boy from eleven to thirteen years of age. This boy was riding on his bicycle, when he met another wheelman coming from the opposite direction. They made two or three attempts to avoid each other, but finally collided; not, however, sufficiently hard to knock either rider from his wheel, and there was no rebounding. The boy dismounted, stood up for a moment, and then dropped dead. Dr. Newton made the autopsy, and found in the middle of the ventricle a small aperture, very like this one which I have shown you to-day. It looked as if a small piece had been torn up. There was no ulceration, fatty degeneration, or thickening of the wall; and that the boy should have been killed by such an insignificant blow seems very strange.

In the average college football match there is not a participant who has not more force applied to his chest than this boy had, and yet such an accident has never been known to occur on the football field. The most reasonable supposition is that the active exercise of bicycle riding had caused his heart to beat very fast, and that the handle-bar of his wheel struck his chest over the heart while the latter was in diastole.

The situation of the tear was, as in my case, in the wall of the left ventricle. Traumatic ruptures do not, however, occur in this locality with the same frequency as they do in spontaneous cases. Gamgee's figures on twenty-eight cases, in twenty-two of which the exact location of the lesion is specified, show that the right ventricle was ruptured in eight, the left in three, the left auricle in seven, and the right in four. Packard has reported a traumatic case which involved both auricles and the interauricular septum. From these figures it would appear that the left ventricle is the least liable to be affected in traumatic cases, while in spontaneous cases the left ventricle is almost invariably the one in which the rupture is to be found.

DISCUSSION.

DR. ANDERS said that in a review of the literature of fatty infiltration of the heart associated with polysarcia he had found only seven cases of rupture. He said that in many instances rupture was not immediately fatal, and that in one case the patient had lived five, and in two others two and three days respectively. He thought it was possible to make the diagnosis during life, and that surgical intervention might then be feasible in selected cases. Rupture occurred in fatty degeneration in about three-fourths of all cases, but also in pure fatty infiltrations and other conditions. In his opinion, this mode of death is of considerable medico-legal importance. *November* 14, 1901.

A Specimen of Bothriocephalus Latus.

DAVID RIESMAN, M.D.

The specimen of *Bothriocephalus latus* which I here exhibit was brought to the nervous clinic of the Northern Dispensary by a Russian woman who seemed to be in very good health and who had been in this country for a number of years. How long she had harbored the worm, or how she had become infested with it, I am unable to say. Unfortunately I have lost sight of her.

Upon examination I found the parasite to be *Bothriocephalus latus;* but, to make sure, I sent some links to Dr. Charles Wardell Stiles, of the Bureau of Animal Industry, Washington, D. C., who was kind enough to inform me that they came from the bothriocephalus.

I placed the worm, which was in several pieces, in alcohol, and did not measure it until it had been in the preserving fluid for a long time. There were altogether about 107 inches—practically three yards (2.72 mm.). I did not come into possession of the head, although it is not unlikely that it was passed. As the first links of the worm are exceedingly tiny, if the head did remain, the body must have been broken off very close to it. The first links that show sexual development measure 3 mm. transversely and 1½ mm. vertically. The mature links near the middle are nearly twice as wide as they are long. They attain an average size of 7 x 4 mm. In each mature link there is a small, dark, bluish spot, centrally located, and slightly projecting from the ventral surface. The lateral incisures denoting the separation of the links are not as distinct as they are in *Tænia saginata;* but, looking down upon the flat surface, the lines of segmentation can readily be seen. The bluish spot, which represents the sexual organs, is placed a little nearer to the anterior than to the posterior end of the link. The color is not uniform in distribution in the area, but is darker in the anterior portion. The branching of the uterus is very simple, and bears some resemblance to a rosette or a Japanese letter. There is no true central stalk, but the branches are distributed somewhat symmetrically on each side of the middle line of the link. In some links I counted from five to seven branches on one side, and from four to five on the other. At the anterior extremity of the rosette there are one or two knob-like projections. The eggs, which are present in enormous numbers, are oval, and have a membrane with a sharp contour. Some are colorless; others are of an olive-green or almost black color. Typical eggs with lids are rare in the links that I have examined. The majority of the ova are either quite homogeneous or look somewhat like a coffee-bean, being composed of two decidedly curved crescents with a clear space between them.

The bothriocephalus is a rare parasite in the United States. So far as I have been able to determine, Dr. Joseph Leidy was the first to find a specimen in this country. The discovery was made in this city in 1879, Dr. J. T. Walker, who presented the worm to Dr. Leidy, having obtained it from a Swedish patient after the administration of a teniafuge. The man passed about fifty feet of worm in the morning, and later in the day passed an additional one hundred feet, weighing 6½ ounces. Dr. Leidy thought that the latter mass represented portions from four or five individuals. Only one specimen is recorded in the TRANSACTIONS OF THE PATHOLOGICAL SOCIETY OF PHILADELPHIA. This was shown by Dr. F. A. Packard in 1891, and had been obtained from a Finnish sailor. If my memory serves me rightly a specimen was also exhibited before this Society by Dr. Stengel, but no record was made of the fact in our TRANSACTIONS.

In 1896, Hagelstam, a practitioner from Finland, temporarily residing in the United States, discovered two cases of bothriocephalus anemia: one in a Finnish woman of Harlem, New York; the other in a lad of twelve years, in Calumet, Michigan.

The bothriocephalus has been known for nearly 300 years, and has in that time received a great variety of names. Its present cognomen is due to Bremser, who, in 1819, gave the first careful description of the worm.

The word bothriocephalus means furrow-head, the term having been applied on account of the two grooves or depressions (*βόθριον*, groove, furrow) on the sides of the head, which take the place of suckers.

In its general surface appearance, the bothriocephalus resembles the other tapeworms; but a careful study by zoologists has shown that it belongs to a species much lower in the scale than the

Tæniadæ. It is simpler in structure, and the individualization of the different parts composing the body is less pronounced than in the latter. The head, for example, is not sharply demarcated from the neck, and hardly represents more than the anterior end of the body provided with an attaching apparatus. The links are also but poorly individualized, and for this reason are more often detached and expelled in the feces in large chains; while in *Tænia saginata* single links are more often discharged.

The alternation of generations is less well defined than in the Tæniadæ, and in some respects the larva resembles the adult, although in *Bothriocephalus latus* the distinction is clear enough. The musculature of the head and of the suckers is simpler than that of other tapeworms, the simplicity consisting principally in the absence of the cup-shaped muscles that characterize the beef and hog tapeworms. In bothriocephalus the sucking muscles are merely parts of the general somatic musculature; the latter, moreover, extends as a continuous strand, instead of being metamerically divided, as in the tenias.

The adult bothriocephalus is from 2 to 9 m. long; the head is almond-shaped, 2 to 3 mm. long, and provided with two deep furrows. The neck is thin and of variable length. The number of proglottids is from 3000 to 4200; they are usually broader than long, at least in the anterior part of the worm. The links have an anterior female and a posterior male surface. On both sides a circumscribed dark-blue area is recognizable, which in the mature links has a star or rosette shape. It corresponds with the egg-filled uterus, which is much simpler in structure than that of the Tæniæ. The genital pore is in the middle of the ventral surface, thus differing from that of the common tapeworm, which is at the margin of the link. The eggs are brownish, elliptical, from 0.068 to 0.071 mm. in length, and 0.045 mm. in width. They are provided with a small lid, which serves to distinguish them from the eggs of other worms. The growth of the bothriocephalus is extraordinarily rapid. Braun found that from thirty-one to thirty-two proglottids, representing from 8.6 to 8.9 cm., are formed in a day. The eggs appear in the feces twenty-four days after the individual becomes infested.

Development. The developmental cycle of the bothriocephalus was for a long time a mystery; but, thanks to the labors of

Braun, Schauinsland, Zschokke, and others, it has at length been determined. The egg of the worm develops into a ciliated, free-swimming larva, known as the onchosphere. From the water it enters the intermediate host, which is some form of fish, particularly the pike (*Esox lucius*) and the burbot (*Lota vulgaris*); also the perch (*Perca fluviatilis*), and perhape the salmon. It infests the intestinal canal, viscera, and flesh of the fish, forming in them a tiny, elongated larva, called the plerocercoid. With the flesh of the fish the larva enters the human intestine, and there develops into the adult worm. The latter has also been found in the dog and in the cat. Both of these, as well as man, are readily infected experimentally by the administration of measled fish. By such experiments Braun demonstrated the fact that various fresh-water fishes are the intermediate hosts of the worms. Autoinfection with the larvæ—*i. e.*, a condition of cysticercus disease, as we see it in *Tænia saginata* and *Tænia solium*—has never been observed in the case of *Bothriocephalus latus.*

Although usually single, it is not rare to find several, and even large numbers, of the bothriocephalus in the same patient. Boettcher found as many as one hundred specimens in the same person; Roux, in one patient, caused the expulsion of ninety, and Heller, in an autopsy upon an old individual, counted thirty-eight specimens. Naturally, when they are so numerous, they are small in size.

Other worms at times coexist with the bothriocephalus in the same intestine.

Distribution. The bothriocephalus has its habitat especially near large lakes; it is common in Switzerland, about Lake Geneva, in Russia, in Scandinavia, and in Eastern Prussia. It is the most common tapeworm in Japan, where both human beings and dogs are inhabited by it. In Belgium, Holland, and France it has also been found. It is said to be frequent in Ireland, and was called by Cobbold the "Irish tapeworm." It has several times been found in Italy. Regarding the United States, I have already shown that it is very uncommon here, although it is likely that, with our enormous foreign population, it will be found more frequently as time goes on.

Effects. Like any other tapeworm, the bothriocephalus may exist in its host without producing any noticeable effects. Often it causes the ordinary group of ill-defined symptoms that we are accustomed to connect with helminthiasis In a certain proportion of cases, however, the bothriocephalus is provocative of a very serious disease, which in every respect resembles classic pernicious anemia.

This effect of the worm was originally pointed out in 1885 by Hoffmann, but the first cases were reported by Reyer in 1886. The condition has since attracted a great deal of attention, as it throws some light upon the pathogenesis of pernicious anemia in general. Schaumann has carefully studied the subject of bothriocephalus anemia, and in a collection of seventy-two cases found a mortality of twelve, or 16.6 per cent. As the worm is not a blood-sucker the anemia is not easily explained. The view now generally held, which was first propounded by Schapiro, is that the parasite elaborates a poison, or that a poison is produced by disease of the worm, or after its death, through decomposition of the dead links. Schaumann and Tallqvist seem to have demonstrated that the links possess toxic properties: by feeding dogs with an extract of the proglottids they were able to produce a decided anemia. Messiner and Calamida also found tapeworm extracts poisonous, although in their experiments the effects were principally of a nervous type. Why only a small proportion of those that harbor the bothriocephalus develop pernicious anemia is not yet explainable. A little light is thrown upon the question by the observation of Schaumann and Tallqvist that there is a decided difference in the toxic action of links from different patients. Whether those obtained from cases of pernicious anemia are more toxic than those from otherwise healthy persons has not been determined, but seems probable.

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DISCUSSION.

DR. STENGEL said that some years ago he had exhibited a bothriocephalus from a Scandinavian sailor in the German Hospital, but had made no report of it. He had also seen another in a foreign sailor, but the specimen had been lost. In the first man there had been no symptoms. The worm was accidentally discovered, but the head was not obtained. He noted that the examination of the stools in bothriocephalus was more difficult than in cases of other tapeworms, as the eggs were not readily discharged and the proglottids did not escape separately. In some cases, as Schapiro had claimed, the worm became diseased and the eggs were discharged. *December* 19, 1901.

A Case of Tuberculosis of the Skin following Accidental Inoculation with the Bovine Tubercle Bacillus.

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The expression of opinion by Professor Robert Koch, at the recent Congress on Tuberculosis held in London, that human and bovine tuberculosis were different diseases and not intercommunicable, gives a special importance to cases in which man has become inoculated with the bovine germ with the production of typical tuberculous lesions. In a former paper before this Society (New Series, vol. iii. p. 259, June 14, 1900) I reported three cases in which men had become accidentally inoculated with the bovine tubercle bacillus while making postmortem examinations. To these I desire now to add a fourth, in which the history throughout is perfectly clear, leaving no doubt as to the bovine origin of the infecting organism.

On July 27, 1901, Dr. G., while performing autopsies on two cows which were the subjects of experimental tuberculosis, wounded the flexor surface of his wrist slightly. Beyond washing thoroughly in water no treatment was adopted, the wound healed promptly, and nothing further was thought of the circumstance until some four weeks later, when the scar was seen to be red, prominent, and somewhat sensitive. It increased in size quite rapidly, and by September 10th there was a nodule in the skin 15 mm. long by 8 mm. in width. On September 14th excision was practised by Dr. Holloway. With a portion of the nodule two guinea-pigs were inoculated subcutaneously, both of which developed generalized tuberculosis. One of them is here presented for the inspection of the Society, the other showing lesions practically identical. Another portion of the nodule was prepared for microscopic examination. Sections stained with hematoxylin and eosin show a round-cell infiltration with a large area of necrosis in the center. Toward the borders of this area are seen numerous giant cells having the nuclei arranged in wreath-like form. The entire process is confined almost wholly to the reticular layer of the corium. In sections stained with carbol-fuchsin an unusually large number of tubercle bacilli are seen, as many as eight being counted in a single field, which is a rare occurrence in tuberculosis of the skin.

The notable features of this case are the rapidity of the growth of the nodule, indicating marked virulence of the infecting organism, and the large number of giant cells and tubercle bacilli seen in the sections. Up to the present time there has been no return of the growth.

Such cases as these do not settle the entire question of the transmissibility of bovine tuberculosis to man, but they prove most conclusively that the bovine germ finds soil and conditions in the tissues of man suitable for its multiplication, and that it produces in man its typical effects, notwithstanding the well-established fact that the skin is by no means a favorable tissue for its development.

In the solution of the problems presented in the relation of bovine and human tuberculosis, patient clinical observation must play a large part, and the report of this case is offered as a contribution to this end. *December* 19, 1901.

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The Etiology of Acute Dysentery in the United States.

E. B. VEDDER

AND

C. W. DUVAL.

(Introduced by S. FLEXNER, M.D.)

ABSTRACT.[1]

It is unnecessary to remind this Society of the investigations of the causes of dysentery carried out in Japan by Shiga, in the Philippines by Flexner and by Strong, and only a few months ago in Germany by Kruse. Before the past summer no systematic attempt had been made to discover the cause of acute dysentery in this country. This undertaking fell to us, and was made possible by a grant from the Rockefeller Institute for Medical Research. Our problem has been (1) to determine by comparative study whether the organisms described by these various observers are not really of the same species, though possessed, it may be, of individual differences and peculiarities, such as may readily exist within the limits of a single species; and (2) to discover the cause of acute dysentery in this country, and if possible to identify it with the organisms of the observers mentioned. If we have succeeded in our undertaking we have gone far toward proving that acute dysentery is the same the world over, and is due to a specific micro-organism, *Bacillus dysenteriæ* Shiga.

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[1] The complete paper appeared in the Journal of Experimental Medicine, vol. vi., No. 2 1902.

The materials at our disposal consisted of the stools of persons supposed to have dysentery and the intestines of several fatal cases of the disease. The stools were examined in the majority of cases, but in some instances the contents of the large gut obtained after death, and scrapings from the diseased mucous membrane were utilized. Plate cultures upon agar-agar were employed. The plates were incubated for twenty-four hours, and then all the colonies were marked with a blue wax-pencil. The plates then were again incubated for another day, and from the new colonies all those which appeared to have the characteristics of *B. dysenteriæ* were inoculated by a simple stab in tubes of glucose agar. In order to select the right colonies a very careful examination with both the naked eye and microscope is necessary, and even then it is hard to exclude positively *B. coli.* Inasmuch, however, as the colon bacillus produces gas in glucose agar, while the dysentery bacillus does not, this step in the technic finally excludes all cultures of the colon bacillus. In explanation of the first step in the process of isolating *B. dysenteriæ*, it may be said that, although among the colonies that have developed after the first twenty-four hours there will be a few colonies of *B. coli*, by far the greater proportion will be of the dysentery bacillus, and that this method renders very valuable assistance in isolating the latter.

The cases studied arose in Philadelphia, New Haven, Conn., and Lancaster, Pa. The Philadelphia cases may be said to have been unfavorable cases for the purposes of our study. The stools and autopsies were obtained from various hospitals in the city, and there was in nearly every instance an unavoidable delay in the transportation of the specimen to the laboratory. It is our belief, judging from the results obtained in these cases, that *Bacillus dysenteriæ* is present in overwhelming numbers in the intestines of patients suffering from dysentery; that the dysentery bacillus does not find the condition in the stool after evacuation so favorable to its growth as does the colon bacillus, and that, therefore, in the stool the latter soon overwhelms the former, and if *B. dysenteriæ* is to be found the fresh stool should be examined immediately. Scrapings from the intestinal mucosa are more favorable than the stool even when freshly collected.

The Lancaster cases were from the Lancaster County Almshouse and Insane Asylum. The epidemic had been very severe, having led to a number of deaths, but at the time of our studies it was on the decline, and only three cases were obtainable. Of these two had been acute, but they had greatly improved under treatment; while the third (Benson) began with symptoms of acute dysentery, which, however, soon subsided, and the attack seemed to have aborted. One of the attacked was an insane patient. The three cases gave positive results.

The New Haven epidemic was the most favorable for study. It occurred at the Springside Home for Paupers and the Insane. The epidemic was very severe, fifty or more cases occurring within three weeks among the 350 inmates, all being of the acute form, with fatalities. The patients were stricken suddenly and were very ill for a few days, their evacuations being extremely bloody and mucoid, containing little or no fecal material, and being odorless during the height of the disease. In all fourteen cases were studied, and from them *B. dysenteriæ* were obtained in large numbers. Several of the stricken were insane patients.

The cultural characteristics of the bacilli obtained from the cases arising in Philadelphia, Lancaster, and New Haven were studied upon all the usual cultural media, and a comparison was made with several standard cultures, to wit: Shiga, from Japan; Kruse, from Germany; Flexner and Strong, from the Philippine Islands. The conclusions which were reached from this study were that the cultural characteristics of the various forms mentioned are essentially alike, for, notwithstanding small individual differences, the variations were so inconstant that it was impossible to distinguish one culture from another.

In morphology the bacillus appears as a slender rod, with rounded ends, about 1 to 3 μ long. It has no tendency to form groups, and is usually found singly, but sometimes in pairs. It stains readily with the ordinary anilin dyes, is not stained by Gram's stain, possesses flagella, and a capsule is sometimes present. Involution forms develop on glucose agar in a very short time, often in twelve hours. Under these conditions the bacilli are very much larger in every way and of strikingly irregular form.

As flagella had not been stained or seen before, a word may be said regarding them and the manner of their demonstration. They are numerous, entirely surround the body of the bacillus, and are eight to ten times its length. They are very delicate, and are arranged in a wavy manner that recalls the delicate hair-line fibrils of floating seaweed. No specific directions for their staining can be given. The following method is the one with which we were most successful, and is a modification of Van Ermengen's method: On an absolutely clean cover-slip place a drop of sterile distilled water, and inoculate this with bacteria obtained from a plain agar culture not more than twelve hours old, being careful not to make too heavy a suspension. Cover the slip carefully to prevent dust from falling on it, and allow it to stand for fifteen to twenty minutes. Dry in the air, without heating at all, and then pass the slip once through the flame for fixation. Now cover the slip with Van Ermengen's solution No. 1, and allow it to remain for two or three hours without heating it, adding enough of the solution from time to time to prevent its drying on the slip. The mordant is to be washed off very gently with distilled water until it is all removed, and without heating the slip the second solution—silver nitrate 0.6 per cent.—is dropped on. This is to remain for five minutes, when it is poured off, and the slip is placed in Van Ermengen's solution No. 3. This is allowed to remain until the color is a light brown (not dark), when it is poured off, and the film is washed again in distilled water and cleared in 1 to 1000 acetic acid and again washed in water, dried, and mounted.

Much time was devoted to the study of the agglutination reactions of the bacilli isolated by us, and at the same time of those cultures with which we first worked, namely, Shiga's, Flexner's, Kruse's, and Strong's. The blood for the tests came from a wide series of cases, including the majority of those from which stools were studied, and some in which stools or autopsies were not obtainable. In addition to the human blood we were supplied with the sample of antidysenteric serum sent by Dr. Shiga to Dr. Flexner. In all cases control tests of the blood sera were made with suspensions of *B. coli* and *B. typhosus,* and normal blood was frequently used as a control for the specific sera. We never obtained an agglutination in any control tests, no matter what dilution was used.

Uniformly positive results were obtained with the blood of dysenteric patients and the antidysenteric serum. Certain variations in the appearance of the clumping were observed. The forms taken by the masses of bacilli may be divided into two groups: In the one the bacteria were tangled in tight bunches, as is commonly seen in the Gruber-Widal reaction; in the other the bacteria were united end to end, and these formed long threads, which were interlaced so as to give rise to a loose skein. This latter appearance has been noted both by Kruse and by Flexner, but it seems to be the exception.

The agglutinating properties do not appear in the blood immediately upon the appearance of clinical symptoms. This is shown by the fact that we had had some patients suffering from undoubted dysentery, from whose stools we secured *B. dysenteriæ,* and yet their blood serum was negative or nearly so.

To sum up the results of this study would be to state that the observations of Shiga made upon the dysenteries in Japan, of Flexner upon the same disease in the Philippine Islands and Puerto Rico, and of Kruse in Germany, can be applied to the acute dysenteries of this country.

The present study also bears upon two other important phases of the problem: the cause of sporadic dysentery, and that of the dysentery of institutions, such as those for the insane. It is also significant that several of the sporadic cases were "terminal" dysenteries. The patients were chronic invalids and had suffered long from chronic Bright's disease, the autopsy establishing the existence of the small contracted kidneys.

The question of motility has been somewhat mooted, in that Shiga, Flexner, and Strong all described some motility, while Kruse has never been able to detect it. Our observations are in this regard in agreement with those of Kruse, although the demonstration of flagella has an important bearing upon the ultimate solution of this question.

CONCLUSIONS.

1. The several standard cultures used in this study are indistinguishable—a conclusion previously reached and stated by Flexner.

2. The acute dysentery of the United States is due to a bacillus indistinguishable from that obtained from the epidemics of dysentery in several other parts of the world.

3. The sporadic and institutional outbreaks of acute dysentery are caused by the same micro-organism, and this organism is identical with that causing epidemic acute dysentery.

4. The cause of acute dysentery, whether sporadic, institutional, or epidemic, is *Bacillus dysenteriæ* Shiga. *December* 19, 1901.

Microchemic Reactions of Tube-casts.

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(PRELIMINARY REPORT.)

Having recently been interested in the microchemic reactions of certain necrotic productions, it occurred to me to study tube-casts by some recent methods. It is not my purpose at the present time to take up the chemistry of renal casts—only to call your attention to certain reactions microchemic in character and directed toward a determination of the chemistry of these bodies. Various views have been held as to the origin and composition of renal casts.

Rovida[1] investigated the origin of these bodies, and looks upon them as secretion products arising from the epithelial cells. This view is adopted by Key.[2] Bayer[3] recognizes their origin from the epithelial cells of the tubules, but looks upon them not as secretion products, but the results of destructive metamorphosis. Meyer's[4] conclusions, antedating the work of Rovida, are practically identical with those of the last-named writer. Langhans[5] adopted both suggestions, believing that certain casts resulted from changes in the epithelial cells and that others were true secretion products. Knoll[6] concluded that chemically, and probably structurally, tube-casts were composed of elements whose nature did not correspond with other known urinary constituents. Traube, Rindfleisch, Klebs, Bartels,[7] and others have taught that the cylinders were really solidified exudates, and Burkart[8] would have us believe that tube-casts were invariably essentially of inflammatory origin. Posner,[9] Torok and Pollak,[10] Neubauer and Vogel, in common with a number of authorities, believe that they are altered albumin that, under the influence of the urine, has solidified in the tubules; and Ribbert[11] came to the conclusion, from experimental studies, that hyaline casts might result from transformation of albuminous exudates. The repeated suggestion that they are fibrin more or less modified has met with disfavor.

Of recent years I am not aware that anything of importance has been added to our knowledge of the origin, structure, and chemistry of these bodies; it has not been my good fortune to add anything startling, but the following experiments have been conducted for the purpose of demonstrating something of the microchemistry of casts.

Technic. Urine obtained as fresh as possible, often within two or three hours after being voided, was rapidly sedimented in the centrifuge, the sediment repeatedly washed with normal salt solution and fixed in the centrifuge tubes by the following methods:* (1) Increasing alcohol, (2) Zenker, (3) Marchi, (4) Müller. The fixed sediment was then stained by a number of methods; hematoxylin alone and with eosin, and also with picric acid; safranin in various combinations, and by a number of mucin stains, among which being that of Paul Mayer.[12] This reagent (muchematein), as originally suggested by Mayer, is probably one of the purest mucin stains that we possess; lately Harris[13] has corroborated this opinion.

Sudan III. and osmic acid have been used for demonstrating fat. The former reagent was applied as follows: Casts fixed in non-alcoholic fixative were thoroughly freed from the reagent and treated with a solution of Sudan III. in 70 per cent. alcohol, washed in water, and mounted in glycerin jelly. Osmic acid yielded much better results, beautiful examples of fat-bearing casts having been obtained by the following technic : Sediment obtained, as already directed, is washed in Müller's fluid and transferred to Marchi's fluid, using the regulation formula of one part of 1 per cent. solution of osmic acid and two parts of Müller's fluid. The reaction usually reaches its height within four or five days, and the casts may be left indefinitely in the fluid.

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* There is no difficulty in fixing, washing, staining, dehydrating (when permissible), clearing, etc., directly in the centrifuge. There is astonishingly little fragmentation of the casts. Staining methods that permit of dehydration are followed by alcohol and appropriate clearing agents, out of which the drop for a balsam mount is taken; methods that require glycerin jelly are simpler, but the results are not permanent.

The muchematein is used according to directions given by Mayer, the watery solution being preferred. It stains more rapidly than hematoxylin, and practically all of my specimens appear to be overstained, although some of them were subjected but a few moments to the action of the stain.

Results. All hyaline casts may be divided into two groups: 1. Hyaline casts that stain faintly with the mucin stain. These casts are usually small, smooth, and free from cells and fat. 2. Hyaline casts that stain intensely, giving the mucin reaction to a degree that renders them almost opaque.

All granular casts in my collection that are not fatty give an intense mucin reaction. Sections of such casts show that the mucin reaction is not restricted to the periphery, but is present in the matrix.

Epithelial casts commonly give a decided mucin reaction, the intensity of which seems to be directly proportionate to the granularity of the cells—the more granular the cells the more evident the mucin stain. Casts of this group are not infrequently found in which one end may show a most intense mucin reaction and cells at the other end give the reaction but faintly—the histologic element (epithelium) staining quite clearly. It would appear the more advanced the degenerative or necrotic change the more evident the mucin reaction; the mucin reaction commonly quite disappears before the advent of fat, as the two reactions have not been observed in the same casts, nor has one been obtained with even the appearance of a second body in another part of the cast.

The origin of the mucin in casts has been considered, but it cannot be said to be definitely determined. Its presence in the epithelial elements of casts and its apparent increase in those undergoing fragmentation and disintegration would seem to indicate that in some way it, at least in part, is a product of necrosis or degeneration, probably both, arising in the cellular elements cast off from the renal tubules. The possibility of cells imbibing mucin from urine rich in some form of the substance has been considered, but does not seem likely. The exact nature of the mucin found in the casts is still undetermined; of the many mucins and pseudomucins known to chemists it is impossible for me to say just which responds to the microchemic tests applied.

Fatty casts are found composed of masses and groups of fat globules possessing slightly different characters depending upon the quantity of fat and the grouping, and held in position by some matrix, the exact microchemic nature of which has not been possible to determine.

1. Some fatty casts are made up almost exclusively of small globular black masses, evidently fat, fairly distributed throughout the length of the cast; in such casts no cellular structure can usually be identified. 2. Casts that contain aggregations of fat usually in the shape of variously sized globules, some of them practically amounting to granules, others nearly the size of nuclei or of epithelial cells. 3. In still another group of casts epithelial cells can be seen the protoplasm of which contains fat. In such cells the fat is usually finely distributed through the perinuclear protoplasm, although I feel quite sure that in some of them it was possible to detect the intranuclear presence of fat.

Observers seem to have agreed that fatty casts result from fatty metamorphosis of renal epithelium, and to this view the observations here recorded offer no contradiction. It seems equally probable that other casts are also the result of necrosis or degeneration of renal epithelium, and that during the progress of the retrograde change mucin becomes a conspicuous constituent. As mucin and fat do not appear to be coincident bodies in the same cast, it would seem reasonable to assume that the presence of one or the other is determined by some condition, the exact nature of which is not apparent. Both may be present in the same urine, but it has not been possible to say why they do not occur strictly together.

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February 13, 1902.

A Case of Hyperplastic Tuberculosis of the Mediastinal Lymph Glands, with Ulceration into the Esophagus, the Left Bronchus, and the Pulmonary Artery.

J. A. SCOTT, M.D.

For clinical purposes tuberculosis of the lymph glands can be divided into generalized and localized tuberculous adenitis.

The first named, generalized tuberculous adenitis, is not a common condition. It is seen more frequently in the negro than in the white man, and sometimes without external lymphatic enlargement or disease of the lung (Osler, p. 282). When the external glands are enlarged the condition may be confused with Hodgkin's disease. A recent investigation has shown that a group of cases diagnosed as Hodgkin's disease has been incited by the *Bacillus tuberculosis*. Weishaupt, Bretano and Fangle, Duclion, Courmont, Texier and Bonnet have all made contributions within the past ten years upon this special form of tuberculous adenitis. Joseph Sailer has recently called attention to a general lymphatic tuberculosis usually preceded by enlargement of the liver and spleen, with final symptoms of ordinary pulmonary tuberculosis, to which symptom-complex he gives the name of Sternberg's disease. The autopsy showed the adenitis to be tuberculous in three cases.

Cases of local tuberculous adenitis are of course too common to be more than mentioned, the commoner group involving the lymphatics of the neck. Reports within recent years, however, have been made of local tuberculous process occurring in the larynx (J. N. MacKenzie), in the intestines (Lartigau), and in the serous membranes, the peritoneum, pleura, and the joints. Reports of tuberculosis of the mediastinal glands have not been wanting. Thus James F. Goodhardt, in the *British Medical Journal*, April 12 and 19, 1879, reports several cases of sudden death occurring in infants or children due to enlargement and caseation of the mediastinal glands. In his cases there was no tuberculous pulmonary condition found, though the mesenteric glands as well were enlarged in one of them. Northrup has reported in 127 consecutive autopsies at the New York Foundling Hospital tuberculosis of the bronchial glands in every case. In Hare's monograph of mediastinal disease we find tuberculosis playing rather a small part in the statistics. It is possible that several of the cases classed as a fibrous hyperplasia may have been tuberculosis. Among the 115 tabulated cases of mediastinal abscess there are 19 that probably are tuberculous, 8 of them being admittedly so, and 11 of them being diagnosed "cold abscess," doubtless tuberculous in origin. The condition found in some of these tuberculous processes is a true hyperplasia, and perhaps the more correct pathologic term for them would be hyperplastic tuberculosis. Lartigau (*Journal of Experimental Medicine*, vol. vi., No. 1), who has reported a case of hyperplastic tuberculosis of the intestines, speaks as follows of the microscopic lesions: "Tubercles may be aggregated in small masses of sufficient size to be appreciated by the naked eye; many showed little tendency to necrotic change. A distinct tendency to fibrous transformation is, on the other hand, apparent. The typical physiologic features of the tuberculous tissues are often absent. In lieu thereof there may exist a diffuse embryonal cell infiltration, at times simulating sarcoma. Tubercle bacilli in the tissues are usually scanty." In his own case of intestinal tuberculosis there is no evidence whatever of pulmonary involvement. This was a fact early noted by the French observers.

The clinical signs of mediastinal tuberculosis are the physical signs common to mediastinal growths. The growth usually occurs from the lymphatics in the middle and posterior mediastinum. The symptoms are generally out of all proportion to the physical signs, while the diagnosis of tumor from aneurysm is at times extremely difficult. The time element is here perhaps very important.

The same pressure symptoms are common to both; pleural effusion is more common in mediastinal tumor than in aneurysm. Dysphagia is an important symptom in mediastinal tumor. It is more common than in aneurysm, and according to Douglas Powell and F. T. Roberts (Allbutt's *System of Medicine*, vol. vii. p. 121) may be the earliest and most prominent symptom. Roberts thinks that where dysphagia is a prominent symptom, where there is an evident growth, the probability is in favor of its mediastinal origin. Tuberculosis of the mediastinal glands may lead to various results. Cases are reported where the growth has involved the superior vena cava, the pulmonary artery, and the azygos vein. A not uncommon result is perforation into the bronchi or trachea, perforation into the esophagus, with at times a production of esophageal pouching. Ulceration into the aorta and pulmonary artery is not common, though such a case has been reported by Sidney Phillips (quoted by Osler). Infection of either lung or subpleural infection may occur. When the glands in the anterior mediastinum and the aorta are involved we may have the production of the pericarditis from rupture into the pericardium of the contents of a caseous gland. Systemic infection may also occur. The following case of mediastinal tuberculosis has recently been under my care at the Pennsylvania Hospital:

Abstract of History. Elizabeth F., colored, aged forty-seven years, widow, a housewife, was admitted to the Pennsylvania Hospital on October 11, 1901 (hospital number, 2300). She had been sent to the ward by Dr. MacCoy because of a left-sided vocal paralysis, the cause of which he wished investigated. The family history was negative; her previous history unimportant. She stated that she had never been sick in her life until four weeks before admission. She married fifteen years ago; husband died shortly after. She had but one child; menopause four years ago, no venereal history. Present illness began four weeks ago with a dry cough of not severe character, which persisted until ten days ago, when it became loose, and was accompanied by expectoration of very viscid, yellowish-white mucus. About the same time the patient started to vomit when she attempted to swallow food or drink. The food seemed to cause coughing, and the coughing produced vomiting. Prior to the coughing she says that she became swollen all over the body. The swollen parts pitted on pressure; in a short time she states the swelling disappeared, being "rubbed away" by her mother. She thinks she has lost about twenty pounds in weight. A few days before admission she had a chill, followed by slight fever. Except for this she has never had any fever. She sleeps well, does not sweat, suffers no pain, bowels are regular. (She is a woman somewhat below ordinary intelligence, and there are some reasons for questioning the reliability of all her statements.)

Physical Examination. Medium-sized colored woman, the skin everywhere rather loose and wrinkled, voice hoarse, pupils equal, pulse rather sclerosed, compressible, regular. Heart dulness, third rib, right border of sternum, apex in fifth interspace midclavicular line. On auscultation nothing of any importance is noted excepting a faint soft systolic murmur heard in the third and fourth right interspaces. The chest is somewhat round, everywhere hyperresonant. The breath sounds are rather feeble, the expiration is decidedly prolonged; there are a few large bronchial rales on both sides, somewhat more numerous on the left. The abdomen is negative; the lymphatics are nowhere enlarged. No visible pulsation at any point of chest, no tracheal tug, no difference in radials. The sputum, which was somewhat small in quantity, was mucopurulent, contained no tubercle bacilli, though pneumococci and streptococci were found. The urine was light yellow, condensed white sediment, acid, 1030, contained neither albumin nor sugar.

On liquid diet she ceased to vomit. Her temperature was usually normal or subnormal in the morning, and 99° at night. The pulse was slightly accelerated, 92 to 100. On the morning of the 19th, one week after admission, she expectorated about four ounces of mucopurulent material, some of it containing tarry or dark-brown blood. Some of the blood clots contained distinct yellowish spots, from the size of a pinhead to a split pea. She complains of no pain; her cough is not brassy, but loose and bronchial in character. I had been carrying two possibilities in my mind as a diagnosis: first, aneurysm or mediastinal tumor; second, esophageal diverticula. The first, aneurysm, was excluded, and I suggested to my resident soon after admission that he pass a soft rubber tube into the esophagus to determine its condition. This was not done until the 11th. Upon the passage of about sixteen inches of the stomach-tube the patient had a violent hemorrhage from the pulmonary artery, which resulted in her immediate death.

The postmortem was made by Dr. Longcope three hours after death. The anatomic diagnosis was as follows: Tuberculosis of superior mediastinal glands; erosion into the left bronchus; perforation into the esophagus; erosion between the left bronchus and the left pulmonary artery; aspiration of blood into the lung; hemorrhage into trachea, esophagus, and stomach; emphysema of lung; splenic tumor; congestion of liver; slight chronic diffuse nephritis; arterial sclerosis; healed tuberculosis of apex of right lung.

The body is that of a poorly-nourished colored woman, 156 cm. in length. Body still warm. Rigor mortis absent; pupils equal. *Peritoneal Cavity.* The omentum is filled with fat, and completely covers the intestines. Peritoneal surfaces smooth and glistening; no fluid. The appendix is patent, free, 4 cm. in length, and lies behind the cecum.

Thorax. Lungs very voluminous and meet in mid-line; no fluid. There are tough adhesions on right side, most marked at apex. Pericardial cavity contains a small amount of clear yellow fluid. Surfaces smooth and glistening. A tumor mass is felt in the superior mediastinum, which appears about the size of an orange. On puncturing the right auricle for cultures, frothy blood exudes, and the heart appears to contain a large amount of air.

Lungs. Left is exceedingly voluminous; the surface is smooth, moist, and glistening, of a mottled gray and purplish color. The air vesicles are enlarged. On section the lung is of a deep-red color, for the most part crepitant, but having in places slight deep-red areas. The bronchi are filled with dark-red blood clots. At the margin of the lung the surface is dry, moderately pale, and the air vesicles are dilated. At the root of the lung the main bronchus is seen to be necrotic at one point. The pulmonary artery adjacent to it is greatly thickened, and at one point is a small erosion through the wall of the artery, which is in direct communication with the necrotic portion of the bronchus. The communication easily admits of passing a match-stick. The small bronchi are somewhat enlarged, and all of them are filled with soft red blood clot. The right lung is densely adherent to the costal pleura; the surface is covered with tough fibrous adhesions. The apex is retracted and very much puckered. On section the apex is densely infiltrated with fibrous tissue, and shows intervening spaces of left lung tissue, dry, pale, and insufflated. The bronchi are dilated. The remainder of the lung is for the most part crepitant, pink in color. In the lower lobe are patches of a deep-red color, which are firm, and slightly raised above the surface of the lung. The bronchi are filled with blood clots. The arteries at the base are clear.

Liver. Size, 22 x 16 x 10 cm.; weight, 1190 grams. The surface is dark brownish-red and covered with a few fibrous tags. Consistence moderately firm. Section gives a mottled brown and red appearance; centers of lobules are red. Bile-ducts patent; gall-bladder filled with thick dark-green bile.

Spleen. Size, 14 x 8 x 4½ cm.; weight, 170 grams. The surface is covered with tough adhesions; capsule wrinkled. On section the spleen pulp is purplish red; Malpighian bodies much enlarged; trabeculæ red and prominent.

Kidneys. Both alike. Size, 11 x 4½ x 3½ cm.; weight, 260 grams. Capsule strips with some difficulty, leaving a finely granular, slightly lobulated, grayish surface. The stellate veins are injected. On section the cortex is pale and cloudy, 6 mm. in thickness; cortical striæ well marked out; glomeruli injected; pyramids dark gray in color. The pelvis contains a moderate amount of fat; ureters apparently normal; adrenals normal.

The heart, aorta, trachea, and esophagus were removed together. The epicardium is smooth, and contains a moderate amount of fat. All the valves are delicate except the aortic, which is slightly thickened. The left ventricle is small; the wall is 18 mm. in thickness; heart's flesh moderately firm and of a brownish-red color. At the base of the heart is a firm mass, consisting of enlarged glands and new growth. The mass is situated between the bifurcation of the trachea, the aorta, and the pulmonary artery. It slightly compresses the superior vena cava, and a projection of the tumor mass can be seen growing into the wall of the vein. The tumor is on section firm, white, and smooth. At its margin it is infiltrating all the surrounding tissues. It follows the left branch of the pulmonary artery and bronchus to the root of the lung. The glands in this area are filled with necrotic masses similar in character to the large growth. To the left of the bifurcation of the trachea is a gangrenous cavity which has eroded the cartilages of the bronchus, and is in direct connection with the left bronchus. The walls of the cavity are lined by necrotic material; foul odor. The external wall of the esophagus directly over this gangrenous cavity is eroded, leaving practically nothing but mucous membrane of the esophagus. This eroded area measures 5 x 2 cm.; the gangrenous cavity measures 2 x 3 cm. In this thin portion of the esophagus, 9 cm. below the isthmus of the thyroid, are two perforations: one the size of a pin-head, with slightly contracted margin; the other 5 mm. in diameter, with perfectly regular rounded edges. Both the esophagus and the trachea are filled with dark-red blood clots.

Stomach contains a large dark-red blood clot, which entirely fills its cavity. Stomach wall apparently normal. The aorta is roughened throughout, and contains yellow roughened plates. Intestines apparently normal; pancreas normal; mesenteric glands not enlarged.

Microscopic specimens of the tumor mass and all the organs were made, as well as sections of the superior vena cava and the left pulmonary artery. The examination of the growth showed the following conditions: The main portion of the mass shows a wide-spread caseation or coagulation necrosis; in each tissue of various kinds are seen, destitute of cellular elements, but preserving their architecture to a certain degree. Surrounding this necrotic area is a narrow zone of epithelioid cells and small round cells, the epithelioid cells being next to the necrotic mass. A few giant cells occur in this zone. Sections of the tumor mass stained for tubercle bacilli have so far failed to reveal their presence. The section of the pulmonary artery shows that the caseating process has advanced up to the median coat. The process also invades at one point the superior vena cava. Epithelioid and giant cells are found. The picture is one which can be considered characteristic of tuberculosis, though we have not been able to demonstrate the presence of the tubercle bacilli. As has been before stated, in these hyperplastic conditions bacilli are more commonly scanty than present in large numbers.

The points of interest in the case may be summed up as follows: A history of five weeks' illness; symptoms of hoarseness, with tendency to cough, and vomiting on ingestion of food. Physical signs very few, owing to the situation of the growth and the marked emphysema present; the extensive ulceration (found at autopsy) into the left bronchus, the esophagus, and the left branch of the pulmonary artery. *December* 19, 1901.

Cancer of Head of Pancreas, with Gallstones.

M. H. FUSSELL, M.D.

Mrs. L., aged fifty-three; married; mother dead of carcinoma of stomach at fifty-four; father of apoplexy. Has five living children, all well. Eight brothers and sisters, all well. Had smallpox when young. No other serious illness. For a number of years patient has noticed what she thought was uterine prolapse. Six weeks ago had pain in abdomen which was not definitely located. No history of severe pain at any time. No jaundice. Two days ago a large rectocele was noticed. This had existed according to history for two weeks. On examination the patient was rather pale, not jaundiced, somewhat emaciated. The rectocele was found, and in the abdomen an illy-defined mass. On percussion there was dulness over lower segment of abdomen; resonance in both flanks.

When patient was turned on side and percussion immediately performed there was resonance in the dependent flank. In the upper portion of abdomen a mass could be felt which apparently floated in liquid. Uterine examination was negative. There was never any history of vomiting.

Blood. Hemoglobin, 75 per cent.; red corpuscles, 4,500,000; white corpuscles, 7500; urine negative. A tentative diagnosis of flaccid ovarian cyst was made.

On January 4, 1902, abdomen opened. About one quart of creamy liquid escaped which was free in the abdomen. The peritoneum was red and lacked luster; there was evidently a peritonitis. The liquid while it was free, that is, it was not encysted, was confined by the coils of intestine which adhered to each other. The solid mass felt before operation was found to be a greatly distended gall-bladder which contained 92 stones. There were several stones impacted in the cystic duct which could not be dislodged. (Owing to condition of patient the duct was not opened.) A mass like enlarged glands was discovered in the mesentery.

Twenty-four hours after the operation the creamy liquid was changed to a liquid resembling olive oil, perfectly clear. The patient was in excellent condition until the fifth day. The bowels were fairly normal. There was positively no vomiting. On the 9th of January jaundice appeared which deepened until death. The patient was in excellent condition until the evening of the 14th of January, ten days after the operation, when sudden persistent vomiting occurred, which lasted until death, on the 15th.

The temperature never rose to 100°, and never was below 97°. The pulse was slow and full until twenty-four hours before death. Examination of the matter vomited showed a creamy liquid containing a few leukocytes. It was not pus, but a changed peritoneal exudate. There were no fat drops.

Postmortem (partial). The original abdominal openings were somewhat enlarged and all observations made through them. The track of the tube left in the wound for drainage is a sinus for about two inches in depth, surrounded by a thick wall; below that the sinus opens into the general abdominal cavity. Coils of the small intestine are adherent to the lower angle of the abdominal wound. The mesenteric glands are greatly enlarged and form stone-like masses. Very numerous areas varying in size from a pin-head to areas one-half inch long by one-eighth inch broad are scattered through the mesentery and over the peritoneum. Some of these masses are cheesy, others contain creamy pus. There is purulent peritonitis. The whole peritoneum is much injected and many patches of lymph are seen, many coils of intestines being adherent with this lymph. The union of the incised gall-bladder with the abdominal wall is firm, and the two are separated with difficulty. A coil of small intestine is tightly adherent to the spot and gas is forced with difficulty past the point of adhesion. A mass consisting of the pyloric end of stomach, portion of liver, gall-ducts, head of pancreas and duodenum, together with numerous enlarged glands, was removed. Examination of portions of this mass show the stomach normal and free from ulceration or induration. The pyloric orifice is normal. The first one and a half inches of duodenum is normal, but just at the flexure and opposite the head of the pancreas the walls are thickened to one-half inch or more, causing a stricture of the gut which barely admits the tip of the finger; the thickening of the wall of the gut is about three inches in length. The head of the pancreas is hard and stone-like.

The wall of the gall-bladder is thickened by inflammatory exudate, and shows the opening of operation wound. Two and a half inches from the fundus is an impermeable stricture. The cystic duct is dilated and contains a number of stones, those not removed at the operation. The papilla marking the entrance of the gall-ducts into the duodenum is somewhat hypertrophied. Through it a probe can be passed into the common duct for the distance of about an inch. There is much inflammatory tissue about the ducts completely occluding the common duct at this point. The cystic duct is absolutely occluded. Examination of various specimens shows the disease to be carcinoma.

A number of points are noticeable in this case:

1. The dearth of symptoms where a necessarily fatal condition existed. Before operation there was no vomiting, no jaundice, but little emaciation. The jaundice in the last days of life was doubtless caused by the rapid occlusion either by new growth or inflammatory thickening about the common duct.

2. The great number of gallstones found in the gall-bladder with occlusion of the cystic duct is but another example of grave cholelithiasis without symptoms.

3. The curious character of the large amount of changed serum. This had the appearance of pus, but contained at first few leukocytes. Later these entirely disappeared.

4. The existence of a grave peritonitis for ten days without fever or rapid pulse. *February* 13, 1902.

Autopsy Findings in a Case of Leprosy.

JAY F. SCHAMBERG, M.D.

The patient was a woman, seventy-seven years old, who first showed evidences of leprosy about eight years ago. Special interest attaches to this case, owing to the fact that the disease was contracted in Philadelphia. The patient had never been outside of this city and its immediate neighborhood. The first manifestation of the disease appeared in the form of a macular pigmented patch upon the back. A section of the skin from this area showed the presence of the bacilli of leprosy. Within the past four or five years distinct bluish-red tubercles, varying in size from a pea to a cherry, have developed upon the face and hands. The skin about the forehead and eyebrows has become infiltrated, thickened, and furrowed, presenting the appearance so commonly seen in tubercular leprosy. The face has acquired a brownish or bronzed tint, which contrasts sharply with the patient's white hair. During the past year the great toes had become ulcerated, but had since healed under the use of antiseptic dressings. The patient died in uremic coma after a week's illness.

Upon autopsy the body was seen to be fairly well nourished, particularly for a woman of such advanced age. Many of the nodules which had been prominent upon the face and hands several months before (the last time that the patient was examined by the writer) had undergone almost complete retrogression and absorption. This was particularly true of the nodules upon the face.

The most conspicuous nodules present were found upon the dorsal surfaces of the first phalanges. These were excised for microscopic study. Upon the face was a pigmented patch about one inch square, which resembled an ordinary patch of chloasma. The skin over the abdomen was harsh, dry, and scaly, and of violaceous hue. The integument of the outer aspect of the legs exhibited bluish-red maculations. The great toes were crusted, but showed no distinct ulcerations.

Heart. The mitral and aortic valves were both hard and atheromatous. The ascending aorta was markedly dilated, measuring one and three-fourth inches in diameter. Large calcified plates were visible in the aorta above the origin of the left carotid artery.

The *lungs* exhibited a high degree of anthracotic pigmentation, but were otherwise normal.

Liver. The liver was about normal in size. On palpation certain areas felt distinctly firmer than others. The anterior inferior surface was whitish, exhibiting a marked thickening of the capsule.

The gall-bladder was small and contained two blackish calculi and a bean-sized cystic mass with yellowish cheesy contents.

Spleen. The spleen was large, measuring seven inches by three and a half inches. Studded upon the surface were numerous pin-head-sized firm nodules of perisplenitis. An irregular depressed scar was seen upon the convex surface. The organ was firm upon section and showed considerable overgrowth of fibrous tissue.

Kidneys. The left kidney was large, measuring five and one-fourth and two and one-half inches. It contained at both extremities four hickory-nut-sized cysts containing clear urine. The cortex was narrow and extremely pale. The pyramids were seen unusually close to the cortical surface, their dark color standing out in strong contrast with the pallor of the cortical tissue. The capsule was much thickened, but could be stripped without tearing. The right kidney was normal in size, but showed the same pathologic conditions as the left.

The other organs showed no alteration of any note.

Microscopic Examination of Tissues. On examining with low power a section of one of the cutaneous tubercles there are seen more or less sharply marginated masses of cells. In the subpapillary layer these take the form of cylindric trails which extend upward toward the papillæ. In the middle of the corium the aggregated masses of cells assume the form of nodules walled off by fibrous connective tissue. The infiltration merges into the panniculus adiposus, and in this region consists both of nodular and diffuse cell arrangement. The cell masses are made up chiefly of fixed connective-tissue cells, although here and there are visible herds of round-cell infiltration. Scattered throughout the corium, with a tendency, however, to locate near the round cells, are seen a number of giant cells. Some of these are typical of the Langerhans cells with the peripheral or segmental arrangement of nuclei, while others belong to the myeloid type. The connective-tissue elements of the corium appear to be increased, forming sharp boundaries for the leprous nodules. The bloodvessels of the corium are considerably dilated and show thickening of their walls. The sweat-glands are in large measure destroyed, their place being taken by a cell-infiltration and fibrous tissue.

Except for the increased vascularity of the corium and the absence of cheesy necrosis, the histologic features might be readily mistaken for lupus vulgaris. Such a view, however, is easily excluded by a bacteriologic examination of the sections. Colored with Gram's stain the skin is seen to contain thousands upon thousands of bacilli.

These are present in the corium wherever there is cell-infiltration. The bacilli are characteristically arranged in clumps. Many are found in cells, while others are seen to be extracellular. Occasionally single organisms are observed to be scattered among the connective-tissue fibers.

Examination of the Chloasma-like Patch of Pigmentation. The appearances under the microscope indicate that this patch was not one of chloasmas, but a true pigmentary lepride. The epidermis is normal save for the excess of pigment in the basal cells of the Malpighian layer. Scattered diffusely throughout the papillary layer of the corium is an infiltration of cells which appear to be of connective-tissue origin. They are loosely arranged with an intercellular fibrous retiform stroma. Scattered here and there are masses of mononuclear and polymorphonuclear leukocytes. There are also visible some giant cells with peripherally arranged nuclei. The cell-infiltration is much more superficial and less dense than in the nodules examined. There is no tendency to extension into the deeper layers of the skin, and consequently the sweat-glands are intact. Bacilli are present, but in much smaller number than in the tubercular lesions.

Spleen. The spleen exhibits an overgrowth of connective tissue and a diminution in size and an irregularity of shape of the Malpighian bodies. Lepra bacilli are found in the spleen both in and between the cells. They show a tendency to clumping in small masses, but not so characteristically as in the skin. The number of bacilli in the spleen is moderate.

Liver. The liver exhibits an overgrowth of connective tissue and a slight tendency to fatty degeneration. *February* 13, 1902.

A Case of Bothriocephalus Latus.

JOSEPH McFARLAND, M.D.

The following case of bothriocephalus infection is of interest not only because of the rarity of the parasite in this country, but because it opens the way for some interesting speculations concerning the age that these parasites may attain and variations in the rapidity of their growth: Mr. S. A. L., aged twenty-two years, a Jew, born in Kurland, Russia, unmarried, a medical student, came to this country eight years ago (1894). Sixteen years ago, when the patient was six years old, he passed four or five yards of tapeworm upon two different occasions. His grandfather, who was a physician, examined the segments, and told him that the tapeworm living in his intestines was a fishworm of a not uncommon kind in that part of the country, but one that was hard to cure. He then prescribed vermifuges and cathartics, which caused the removal of several more yards of worm. The boy was made ill by the medication, and it was not repeated. However, from this time no signs of the worm appeared, and six or seven years passed, during which time it was believed to be dead.

The patient had been in this country but a short time when, after having eaten of an unusual food, which caused rather active diarrhea, he was astonished to find in the feces which had been passed a considerable piece of tapeworm, consisting of the larger segments. Nothing was seen of the worm for six months or more, when about a yard or two was passed upon a similar occasion, and from this time on the patient says that once or twice a year, usually in the spring and autumn, at times when there is a change in the family table, depending upon the advent of fruit, berries, and other vegetable foods, sometimes a yard or two or several yards of the worm will be passed.

During all the years since he became host to the parasite, the patient has never experienced any unpleasant sensation, or any illness, or anything to call his attention to the fact that he is host to the tapeworm. The last piece of tapeworm, which is presented for your examination this evening, was passed at an interval of one and a half years, and usually succeeded mild diarrhea. Since the passing of this fragment the patient has taken a number of very active vermifuges, followed by powerful cathartics, but has not discovered any other segment of the worm. The patient is below normal stature, his complexion is pale, contrasting with the very dark hair and eyes of his race. He is slight, but not feebly built, and considers himself to be in perfect health. An examination of the blood made in the Clinical Laboratory of the Medico-Chirurgical College gives the following results: hemoglobin, 80 per cent.; erythrocytes, 4,760,000; leukocytes, 86,000.

The examination of the worm confirms the diagnosis made by the patient's grandfather so many years ago, and shows it to be the bothriocephalus latus.

It would be interesting to know whether the worm, the segment of which was periodically passed at the present time, is the same worm originally seen by the patient's grandfather sixteen years ago, or whether that worm was killed as a result of his medications, passed unobserved, and the present worm another subsequently developed in the patient. It seems rather remarkable that the worm should remain with its presence unnoticed for seven years, yet the subsequent history of this worm, that fragments shall be passed only at prolonged intervals—intervals varying from six to eighteen months—shows it to be of very slow growth, while the good health enjoyed by the patient and the result of the examination of his blood would seem to indicate that the worm was not very active.

Upon carefully questioning the patient concerning his habits, it was learned that raw fish is not eaten in the part of the country from which he comes unless it be well smoked, and that of the smoked fish, especially herring, considerable quantities are consumed.

Very little accurate information bearing upon the subject of infection could be secured from the patient, so that nothing more can be said about it than that it probably resulted from eating smoked fish. It has been shown by numerous investigators that smoked fish may contain the live embryos of this worm, and that for their destruction a more considerable heat than that germinated by the smoke fires is necessary.

It is of course well known that the bothriocephalus is a common parasite in Sweden, Norway, Russia, and the countries about the Baltic Sea, and as the grandfather of the patient said, when the parasite first made its appearance, it was the form of a tapeworm quite common in that part of the country. *February* 13, 1902.

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Second Annual Exhibition Meeting of the Pathological Society of Philadelphia.—HARE and ROSENBERGER, Saccular Aneurysm Arising from the Ascending and Transverse Parts of the Arch of the Aorta.—LONGCOPE, Streptococcus Mucosus (Howard) and its Relation to Micrococcus Lanceolatus.—JUMP and STEELE, Primary Carcinoma of the Liver.

Second Annual Exhibition Meeting.

The Pathological Society of Philadelphia last year inaugurated the custom of holding an annual exhibition meeting, designed to illustrate the progress of pathology and to bring before the members in an objective manner pathologic subjects of contemporary interest. At the second meeting, held in the Mütter Museum of the College of Physicians, on January 9, 1902, a large number of gross and microscopic specimens, covering a wide range, were exhibited. The meeting was largely attended. A list of the specimens shown, together with the names of their exhibitors, is given below:

Dr. A. C. Abbott, Department of Hygiene, University of Pennsylvania.

1. Tubercle-like nodule in lung of rabbit. Animal killed thirteen days after intravenous injection of pure culture of Moeller's grass bacillus II.

2. Miliary tuberculosis in lung of rabbit. Animal killed twenty-nine days after intravenous injection of pure culture of Bacillus tuberculosis.

3. Experimental tubercle-like nodule in kidney. Showing actinomyces-like development of Moeller's grass bacillus II.

4. Tubercle-like nodule in lung of rabbit. Animal killed

thirteen days after intravenous injection of pure culture of Moeller's grass bacillus II.

5. Pure culture of Moeller's acid-proof grass bacillus II. Seventy-two hours old, in glycerin agar-agar at 37° C.

6. Tuberculosis of the kidney in rabbits. Miliary tubercles twenty-nine days old.

7. Miliary tuberculosis in lung of rabbit. Animal killed twenty-nine days after intravenous injection of pure culture of Bacillus tuberculosis.

8. Tubercle-like nodule in lung of rabbit. Animal killed thirteen days after intravenous injection of pure culture of Moeller's grass bacillus II.

9. Miliary tubercle in kidney of rabbit. Animal killed nineteen days after intravenous injection of pure culture of Bacillus tuberculosis, showing early stages of development.

10. Tubercle-like nodule in kidney of rabbit. Animal killed twelve days after intravenous injection of Moeller's grass bacillus II., showing early stages of development.

11. Tuberculosis of the kidney in rabbits. Miliary tubercles twenty-nine days old.

12. Tubercle-like nodules in kidney of rabbit. Result of intravenous injection of Moeller's grass bacillus II.

13. Experimental miliary abscess of kidney—for a comparison with tubercle and tubercle-like nodules. Three days after intravenous inoculation with Staphylococcus pyogenes aureus.

14. Miliary abscess of lung, showing embolus of bacteria. Specimen loaned by Dr. William Pepper.

Dr. R. A. C. Buckley, Medico-Chirurgical College.

Metastatic Cancer of the Spine. Series of sections from different levels.

Drs. W. M. L. Coplin, Ward Brinton, and **W. B. Eaton,** Jefferson Medical College Pathological Laboratories.

1. Thrombophlebitis (vein of leg) and thromboendarteritis of accompanying artery. Case of senile gangrene involving foot and lower third of leg.

2. Gumma of heart.

3. Interstitial and peripancreatic hemorrhage from dog. Clinical history not known. Found in animal killed for dissection.
4. Granulomas (?) of calf's heart.
5. Chronic phagedena of penis. (Gross specimen.)
6. Chronic phagedena of penis, etc. Stained with hematoxylin, followed by Van Gieson's method.
7. Hyperplasia of adrenal.
8. Carcinoma of adrenal.
9. Healing wound of liver and abdomen.

Dr. M. H. Cryer, University of Pennsylvania.

1. Mandible, with cortical portion of bone removed, exposing the cancellated tissue and the cribriform tubes.
2. Anterior view of a vertical transverse section of the head, showing the relation of the jaws and the U-shaped cortical bone of the mandible, also indicating the position of the turbinates, antrums, etc.
3. View of mandible (left side), with cortical portion of the bone removed along with the cancellated tissue, exposing the nerves and vessels within the cribriform tubes as they pass to the roots of the teeth.
4. Posterior view of a vertical transverse bilateral section of the head, showing the ostium maxillare, which is indicated on each side by a cord passed through it.
5. Section showing greater portion of the upper jaw. S. S. sounds passed down lacrimal duct, showing that they do not pass at the same angle. There is also an impacted canine tooth.
6. Horizontal section, showing the under surface of the inferior turbinates and the outlet of the lacrimal duct.
7. Two anteroposterior sections made by dividing the orbit and maxillary sinus vertically, showing conical elevations over the roots of the various teeth. The root of the second premolar curves forward. It more commonly curves backward.
8. Anteroposterior division through the center of the orbit, maxillary sinus, and teeth, showing an enlarged cell in the orbital process of the palate bone and a correspondingly small maxillary sinus.
9. Anteroposterior division through the center of the orbit,

maxillary sinus, and molar teeth, showing a large maxillary sinus and a large sphenoidal sinus.

10. External walls of right and left nasal chambers, showing four meatuses and a partial fifth.

11. Two views of an anteroposterior section, showing the inner wall of the orbit, maxillary sinus, and openings leading into the sphenoidal sinus and the external wall of the nose and a large sphenoidal sinus.

12. Anteroposterior division of the maxilla, showing opening of a dental abscess within the antrum and an infraorbital sinus.

13. Horizontal section above the right floor of the nasal fossa and maxillary sinus, showing the opening of a dental abscess in the floor of the antrum.

14. Large frontal sinuses, extending from one external angular process of the frontal bone to the other.

15. Posterior view of a vertical transverse section of skull in region of second premolar, showing lack of symmetry in the nasal fossæ and maxillary sinuses, with the septum and "spur" passing over the inferior turbinate.

16. Anterior view of a vertical transverse section, showing lack of uniformity in the two maxillary sinuses.

17. Anterior view of a vertical transverse section near the first premolar, showing variations in the maxillary sinuses and the nasal fossæ.

18. Posterior view of two vertical transverse sections made from different skulls in about the same anatomic region, showing great variation as to depth of face and size and shape of the maxillary sinuses and nasal chambers.

19. Posterior view of two vertical transverse sections made from different skulls in about the same anatomic region, showing great variations as to depth of face and size and shape of nasal and maxillary sinuses.

20. Anterior and posterior views of a vertical transverse section in the region between the second premolar and first molar teeth, showing a wire passing from the frontal sinus into the maxillary sinus. The frontal sinus extended downward to nearly the level of the upper portion of the antrum.

21. Posterior view of a vertical transverse section near the first

molar teeth, showing maxillary sinuses which are nearly cuboidal in shape and which extend downward below the floor of the nasal fossæ. The nasal chamber is narrow, and the walls dividing it from the sinuses are concavoconvex in their vertical direction.

22. An impacted canine tooth, the crown in the roof of the mouth, the greater portion of the root in the maxillary sinus.

Dr. W. B. Eaton, Jefferson Medical College.

1. Myoepithelioma of uterus.
2. Red atrophy and focal necrosis of liver.
3. Lardacein reaction in liver. Stained with hematoxylin, fuchsin, and anilin blue.
4. Lardacein reaction in spleen. Stained with fuchsin and anilin blue.
5. Hemorrhage of adrenal (coagulation necrosis).
6. Tuberculosis of adrenal.

Dr. S. Flexner, Pathological Laboratory, University of Pennsylvania.

1. Tuberculosis of larynx (3).
2. Tuberculosis of uterus and Fallopian tubes.
3. Splenomegaly (2) (Banti's disease).
4. Multiple thrombi of aorta.
5. Osteomyelitis of tibia.
6. Rupture of varicose esophageal veins; cirrhosis of liver.
7. Acute hemorrhagic pancreatitis in dog (experimental).
8. Tuberculous pericarditis.
9. Tuberculous ulcer of bladder.
10. Thrombus in aorta.
11. Multiple hemorrhages beneath pericardium.
12. Malignant adenoma of uterus.
13. Chronic internal hemorrhagic pachymeningitis.
14. Acute fibrinous pericarditis.
15. Charcot joint.
16. Aneurysm of arch of aorta.
17. Thrombosis of coronary artery; infarction of heart.
18. Thrombosis of both pulmonary arteries.

Drs. Hansell and **Le Fever.**

1. Staphyloma of cornea, with prolapse of vitreous.
2. Hemorrhagic glaucoma.
3. Non-purulent panophthalmitis; twenty years after injury.
4. Acute hemorrhagic glaucoma.
5. Staphyloma of cornea. This condition followed an attack of scarlatina.
6. Suppurative panophthalmitis, following a penetrating wound.
7. Bone in vitreous humor; followed gunshot wound of six years' standing.

Dr. Addinell Hewson, Jr.

Syphilis of skull.

Dr. Wilmer Krusen.

Triple ectopic gestation (second month). Patient aged thirty-four years; operation; death following forty-eight hours later. Gross specimen fixed with formalin; then placed in Galt's solution.

Dr. Lapham.

1. Golgi preparation of brain of rat.
2. Injected villi of intestine of cat.

Dr. Joseph Leidy, Jr.

Specimen showing appendicular portion of the cecum (so-called second stomach) from a lemur, closely allied to man.

Dr. Longcope, Ayer Clinical Laboratory, Pennsylvania Hospital.

1. Extreme arterial sclerosis.
2. Periosteal sarcoma of femur.
3. Tuberculous ulceration between pulmonary artery and left bronchus.
4. Metastatic carcinoma of ribs.
5. Incarceration of appendix in hernial sac, with carcinomatous nodules over appendix.
6. General carcinomatosis of peritoneum.
7. Primary carcinoma of gall-bladder, cholelithiasis, and extension of carcinoma.
8. United fracture of femur.

Drs. D. J. McCarthy and **M. P. Ravenel,** Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

1. Rabic tubercle of Babes in the oblongata, due to a pericellular accumulation of embryonal cells about the ganglion cells.

2. Intervertebral ganglion of cow with rabies. Vacuolation of ganglion cells and pericellular and intracapsular cell proliferation.

3. Plexiform ganglion of dog, showing typical lesions of rabies. The cell capsules are proliferated and fill up the capsules.

4. Intervertebral ganglion of a cow. Each cell is surrounded by a capsule of a single layer of cells.

Dr. D. J. McCarthy, Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

1. Sarcoma of right occipital lobe of brain.

2. Sarcoma of the temporosplenoidal lobe, with secondary involvement of the piaarachnoidal membranes.

3. Fibrosarcoma of right Rolandic area. Depression is shown over the leg center.

4. Cystic sarcoma of the cerebellum. The vermis and lateral lobes are extensively involved.

5. Brain abscesses following operation for subdural hemorrhage.

6. Ependymoma. Sarcomatous multiple growths originating from the lining of the ventricles.

7. Hyaline exudates, filling the third and fourth brain ventricles. Tumor mass is stained black and affects the centrum semiovale and corpus callosum.

8. Hyaline exudate as a tumor formation lying free in the third brain ventricle.

9. Embolus of branch of right Sylvian artery supplying Rolandic area.

10. Multiple tuberculous growths of the brain. The under surface exhibits an isolated tumor of the left cerebral peduncle.

11. Chronic internal hydrocephalus.

12. Glioma of the pituitary body, penetrating the third and extending to the fourth ventricle, through the aqueduct of Sylvius.

13. Associated gliosis and syringomyelia in the spinal cord.

14. Endothelioma of the superior motor area. The depression from which the tumor was removed is seen on the convexity.
15. Melanosis of pia over pons and medulla.

Drs. J. McFarland and **W. Wayne Babcock,** Medico-Chirurgical College, Pathological Laboratories.

1. Normal kidney. Injected.
2. Amyloid kidney.
3. Amyloid kidney, with calcareous deposits.
4. Amyloid kidney, with chronic parenchymatous nephritis.
5. Hemorrhagic infarction of kidney.
6. Gonorrheal pyemic kidney. Renal infarction.
7. Pyelonephrosis—wall of abscess.
8. Abscess of kidney, showing masses of bacteria.
9. Necrosis of kidney. Twenty-four hours after ligation of renal artery.
10. Miliary tuberculosis of kidney without giant-cell formation.
11. Miliary tuberculosis of kidney, showing giant cells.
12. Parenchymatous nephritis, acute.
13. Anthrax. Bacilli in renal glomerule.
14. Metastatic abscesses in kidney.
15. Acute parenchymatous nephritis.
16. Hypernephroma.
17. Carcinoma of kidney.
18. Endothelioma of uterus.
19. Columnar carcinoma of kidney.
20. Papillary epithelioma of kidney. (Originated in renal pelvis.)
21. Metastatic round-cell sarcoma in the kidney.
22. Angiosarcoma of kidney.
23. Pseudoleukemia—kidney.
24. Arteriosclerosis of kidney.
25. Chronic interstitial nephritis.
26. Chronic interstitial nephritis, with calcareous deposits.
27. Chronic interstitial and parenchymatous nephritis.
28. Acute parenchymatous nephritis. Desquamation.
29. Catarrhal nephritis.

Dr. C. K. Mills.

Calvarium and brain from case of internal hydrocephalus, with symptoms of cerebellar tumor.

Dr. F. Savary Pearce.

1. Apoplectic cyst. Specimen from Museum of the Philadelphia Hospital.
2. Tumor of pineal body. Specimen from Museum of the Philadelphia Hospital.
3. Extradural hemorrhage. Specimen from Museum of the Philadelphia Hospital.
4. Hemorrhage into brain.
5. Hemorrhage into internal capsule.
6. Tumor of hypophysis.
7. Tumor of infundibulum.
8. Tumor of the cerebrum.

Dr. L. H. Prince.

1. Hypernephroma of kidney.
2. Tumor of spleen from a dog.
3. Skin from a case of variola.
4. Hypernephroma of kidney. Fixed in Kaiserling's solution.
5. Endothelioma of pituitary body.

Dr. B. Alex. Randall.

1. Caries of tympanum and petrous portions of temporal bone, causing cavernous sinus thrombosis. Nearly complete bony healing of mastoid trephining done one year before.
2. Carious temporal trephined for the relief of lateral sinus thrombosis thirty years ago by Dr. Samuel Ashhurst at the Episcopal Hospital.
3. Absorption of the walls of the external auditory canal, with opening of the adjacent mastoid cells, probably due to pressure of a large polypoid growth.
4. Thrombotic jugular vein deligated and excised entire, with evacuation and partial excision of the lateral sinus, for otitic phlebothrombosis.

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5. Tubercular caries of tympanum, with sequestrum forming in mastoid. Negro girl of seven years.

6. Colored plastic sketches of normal and pathologic drumhead conditions for demonstrating purposes.

7. Portions of two rhinoliths broken in removal, and a shoe button and thread, with calcareous incrustation, illustrating the usual formation of such concretions. (All from patients at the Children's Hospital.)

Dr. M. P. Ravenel, Laboratory of the State Live-stock Sanitary Board of Pennsylvania.

1. Larynx of horse from case of forage poisoning, formerly called cerebrospinal meningitis.

2. Glanders. Nasal septum of horse.

3. Osteoma of lung of horse.

4. Tuberculosis. Lung of cow inoculated in the jugular vein.

5. Tuberculosis. Lung of cow, showing cavity formation. The animal was infected experimentally by feeding.

6. Tuberculosis. Larynx of cow.

7. Tuberculosis. Mediastinal gland of cow.

8. Tuberculosis. Lung of calf infected by intravenous inoculation of pure culture of tubercle bacillus obtained from mesenteric gland of child.

9. Tuberculosis. Lung of calf infected by intraperitoneal inoculation of pure culture of tubercle bacillus obtained from mesenteric gland of child.

10. Tuberculosis. Section of lung of calf inoculated intravenously with culture of tubercle bacillus isolated from mesenteric gland of child.

11. Tuberculosis. Section of liver of calf inoculated intravenously with culture of tubercle bacillus isolated from mesenteric gland of child.

12. Tuberculosis. Liver of calf infected by intraperitoneal inoculation of pure culture of tubercle bacillus obtained from mesenteric gland of child. The liver is adherent to diaphragm. The thickened omentum is seen adherent to anterior surface of liver.

13. Tuberculosis. Spleen of calf inoculated intraperitoneally with human sputum.

14. Forage poisoning. Pharynx of calf.

15. Verminous pneumonia of calf.

16. Pneumonomycosis. Lung of heifer.

17. Trachea of calf showing Strongylus filaria.

18. Tuberculosis. Lungs of pig fed with pure culture of human tubercle bacillus. From same animal as tonsils in next jar.

19. Tuberculosis. Tonsils of swine infected by feeding pure culture of human tubercle bacillus. Ten feedings were given, 5 c.c. of milky suspension of the culture being given each time.

20. Intestinal parasitism of hog.

21. Intestine of hog showing gaseous bullæ.

22. Hog cholera. Intestine of hog, showing necrotic ulcers characteristic of this disease.

23. Tuberculosis. Peritoneum of guinea-pig.

24. Tuberculosis. Spleen of guinea-pig following subcutaneous inoculation with pure culture of human tubercle bacillus.

25. Tuberculosis. Lung of rabbit following subcutaneous inoculation with pure culture of human tubercle bacillus of high virulence.

26. Tuberculosis. Liver and spleen of monkey following subcutaneous inoculation with bovine tubercle bacillus.

27. Tuberculosis. Section of nodule from case of skin tuberculosis due to accidental inoculation with bovine tubercle bacillus.

28. Colloid goiter of hyena. Pure cultures of the streptococcus were obtained from the cysts, and sections show the same organism.

29. Aneurysm of axillary artery of chicken, probably traumatic.

30. Caseous lymphadenitis of sheep. Lung.

31. "Acid fest" and proof bacilli.

32. Culture of tubercle bacillus from various sources, and some of the "acid fest" and proof group.

33. Cultures of tubercle bacillus from various sources and some of the "acid fest" group of bacilli.

Drs. R. C. Rosenberger, Bradeen, and **Graham,** Jefferson Medical College.

1. Congenital cystic disease of kidney.

2. Specimens in Galt's solution. Note the normal consistency

of the organs. The solution consists of sodium chlorid, 150 grams; chloral hydrate, potassium nitrate, āā 30 grams; water, 300 c.c. Specimens are first thoroughly washed in water, then placed in alcohol, 95 per cent., or formalin, for one or more days, and finally placed in the solution. If the solution evaporates simply add water.

3. Thrombophlebitis of renal vein, Gross. (Septicemia following laparotomy.)

4. Thrombophlebitis of renal vein, sections of.

5. Trichinella spiralis in muscle.

6. Hyperplasia of adrenal.

7. Liver-like tissue in adrenal.

8. White rat, spindle-cell sarcoma of thigh. No metastases were in the internal organs.

9. Sections of spindle-cell sarcoma from white rat.

10. Tænia saginata, malformation of. Gross specimen.

11. Malformation of heart. Communication between the ventricles immediately below the aortic cusps. The pulmonary artery arises from the right ventricle; the aorta from both ventricles.

Dr. Jay F. Schamberg.

Specimens of smallpox eruption. Fifth to tenth day.

Dr. G. E. de Schweinitz.

1. Traumatic iridocyclitis, showing exudate in the ciliary region and behind the lens which forms the so-called cyclitic membrane; numerous round-cell foci throughout the retina.

2. Pigmented sarcoma of the choroid of unusual cake-like formation.

3. Complete staphyloma of the cornea following gonorrheal ophthalmia.

4. Leukosarcoma of the choroid.

5. Traumatic iridocyclitis, with detachment, thickening, and cystic degeneration of the retina.

6. Metastatic carcinoma of the choroid.

7. Shrunken eyeball with ossification of choroid.

8. Normal eye.

9. Traumatic iridocyclitis.

10. Traumatic iridocyclitis following foreign body in the eye; hemorrhage in vitreous and anterior chamber.

11. Glaucomatous degeneration of an eyeball; hemorrhage posterior to the cataractous lens. Secondary glaucoma and ciliary staphyloma; deep cupping of disk.

12. Gumma of the ciliary region.

13. Shrunken eyeball after slag burn of the eye.

14. Glioma of the retina.

15. Complete leukoma of cornea following abscesses, with hemorrhage into the anterior chamber.

16. Deeply pigmented, spindle-cell sarcoma of the corneoscleral junction.

17. Phthisis bulbi following gonorrheal ophthalmia.

18. Sarcoma of the corneoscleral junction.

Dr. Edward A. Shumway.

1. Koch-Weeks bacillus. Acute catarrhal conjunctivitis (contagious). From Pepper Laboratory of Clinical Medicine.

2. Myopia; extensive choroiditis. From Pepper Laboratory of Clinical Medicine.

3. Retrobulbar sarcoma; female, aged sixty-seven years.

4. Alveolar sarcoma of the choroid; female, aged seventy-one years.

5. Hemorrhagic glaucoma; female, aged fifty-four years. Last stage, with rupture of the globe and extensive intraocular hemorrhage.

6. Staphyloma of cornea, following gonorrheal ophthalmia in child.

7. Carcinoma of eyelids, with secondary involvement of cornea and sclera. Perforation of the sclera. Absolute glaucoma. Extensive intraocular hemorrhage.

8. Atrophy of the eyeball following burn of the cornea.

9. Hemangioma cavernosum of orbit. Child, aged three years. The tumor possessed a thick capsule and gave no thrill or bruit.

10. Panophthalmitis. Iron fragment in the vitreous cavity.

11. Subretinal cysticercus.

12. Glioma of the retina. Male, aged three years. Death three months later from recurrence locally and in the brain.

13. Sarcoma of choroid.
14. Tuberculosis of choroid.

Dr. William G. Spiller, Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

1. Normal oculomotor nuclei.
2. Cervical region in amyotrophic lateral sclerosis.
3. Spinal syphilis. Numerous miliary gummata and round-cell infiltration.
4. Intense neuritis. Method of Azoulay.
5. Anterior poliomyelitis. Sclerotic area of left anterior horn.
6. Syringomyelia.
7. Intensely atrophied hypoglossus nucleus in amyotrophic lateral sclerosis.
8. Normal hypoglossus nucleus.
9. Cervicobulbar tabes.
10. Disseminated sclerosis. Cervical region : secondary degeneration in crossed pyramidal tract of lumbar region. Medulla oblongata: involvement of oculomotor nuclei.
11. Concussion of spinal cord. Middle cervical region : degeneration in the ascending tracts. Lumbar region : degeneration in crossed pyramidal tract extending from the lower cervical region.
12. Disseminated sclerosis. Degeneration in right anterior horn; degeneration in posterior columns on each side in area of patellar reflex arc.
13. Early tabes. Cervical region: Degeneration of posterior columns is slight. Lumbar region: Degeneration of posterior columns (slight).

Drs. Courtland Y. White and **William Pepper**, Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

1. Erythrocytes. Normal. Normal blood.
2. Erythrocytes. Normoblast. Secondary anemia.
3. Erythrocytes. Normoblast showing karyorrhexis.
4. Erythrocytes. Macroblast showing pyknosis of nucleus. Pernicious anemia.
5. Erythrocytes. Macroblast showing karyokinesis. Pernicious anemia.

6. Erythrocytes. Granular or basic degeneration. Chronic lead poisoning. Two specimens.

7. Erythrocytes. Megalomacroblast showing karyolysis. Pernicious anemia.

8. Erythrocytes. Microblast. Pernicious anemia.

9. Erythrocytes. Poikilocytosis. Pernicious anemia.

10. Erythrocytes. Anisocytosis. Secondary anemia.

11. Erythrocytes. Gigantoblast, showing karyolysis. Pernicious anemia.

12. Leukocytes. Normal. Lymphocyte, transitional and mononuclear forms.

13. Leukocytes. Normal, polynuclear, eosinophile. Mycosis fungoides.

14. Leukocytes. Vacuolation.

15. Leukocytes. Acidophilic or eosinophilic myelocyte. Splenomyelogenous leukemia.

16. Leukocytes. Leukocytic shadows.

17. Leukocytes. Neutrophilic myelocyte. Splenomyelogenous leukemia.

18. Leukocytes. Basophile.

19. Splenic myelogenous leukemia.

20. Acute lymphatic leukemia.

21. Splenomyelogenous leukemia.

22. Chronic lymphatic leukemia.

23. Malaria. Estivoautumnal form (crescents).

24. Malaria. Tertian form.

25. Filaria sanguinis hominis.

26. Jenner and Ehrlich (triple) stain. Splenomyelogenous leukemia.

Dr. George B. Wood.

1. Endothelioma of nasal fossa.

2. Lacunar keratosis of lingual tonsil, with leptothrix and other organisms. Leptothrix, stained blue, grown from frayed keratotic mass.

3. Lacunar keratosis of faucial tonsil. Keratoid mass projecting from crypt, which is surrounded by small quantity of tonsil parenchyma.

Saccular Aneurysm Arising from the Ascending and Transverse Parts of the Arch of the Aorta.

H. A. HARE, M.D.,
AND
RANDLE C. ROSENBERGER, M.D.

(*From the Laboratories of the Jefferson Medical College Hospital.*)

Anatomic Diagnosis. Red atrophy of the liver; aneurysm of the ascending aorta; edema and congestion of the lungs; chronic interstitial nephritis; chronic pleuritis.

Body of a well-nourished female, aged forty-eight years; edema of face, especially beneath the eyes. Small areas of ecchymosis over the chin; suggillation well marked in back and buttocks; cyanosis of the lips and finger tips. Rigor mortis well marked in both the upper and lower extremities, but easily broken up. The fat of the abdominal wall is abundant and normal in color; musculature normal. The abdominal organs are normal in situation; the peritoneal cavity contains 200 c.c. of clear fluid. There is a fibrous adhesion binding the left lobe of the liver to the under surface of the diaphragm.

The left pleural cavity contains 60 c.c. of clear, reddish fluid; old adhesions are present at the base of the lung, and recent adhesions at the apex. The right pleural cavity contains 60 c.c. of clear reddish fluid; there are numerous old adhesions, especially at the base of the lung. The pericardial cavity contained about 200 c.c. of fluid blood and several large currant-jelly clots, the total volume of the latter equalling 250 c.c. The membrane is slightly thickened and the visceral layer is roughened in a few small areas over the left ventricle. About 2.5 cm. from the aorta and immediately posterior to the superior vena cava is an irregular jagged opening 1 cm. in length and 5 mm. in width, occupied by a clot and forming a communication between the pericardium and the cavity of the aneurysm. The extreme apex of the heart is covered by a fibrinous mass 5 mm. in thickness; upon the right ventricle is a milk spot 2.5 cm. in diameter. The subepicardial fat is excessive, particularly over the right ventricle and along the line of the septum. The coronary vessels are tortuous, prominent, and atheromatous. The heart is small; the myocardium is firm, and normal in color and consistence. No valvular lesions are present. The cavities are empty, and, with the exception of the right auricle, which is slightly dilated, there is no conspicuous abnormality in their capaciousness. Both lungs are edematous and congested. The mucosa of the trachea and bronchial tubes is hyperemic, the hyperemia being particularly evident in the smaller bronchi.

The spleen is flabby, dark-red in color, and presents a concavity upon the external end and four fissures on the anterior edge. The pulp is slightly softer than normal. Weight, 170 gms. The left adrenal is apparently normal. The left kidney is small, narrow, and lobulated; small areas of fibrosis are seen upon the anterior aspect; it cuts with resistance. The cortex is pale and narrowed in areas, normal in other areas; the pyramids are congested; an abundance of fat is present in the pelvis. The capsule strips with resistance. One small cyst, 5 mm. in diameter, at the cortico-medullary junction, is also observed. Weight, 130 gms. The right adrenal is apparently normal. The right kidney is smaller than its fellow; the cortex is pale, narrow in some parts, and apparently normal at other points. The medullary portion contains no evident gross lesions. Weight, 100 gms. Ureters and bladder normal. The liver is slightly smaller than normal, dark-red in color; the surface is smooth, the edges slightly rounded. The left lobe is small, flat, and tapering, and is attached to the diaphragm. The gall-bladder extends below the margin of the organ; it contains 15 c.c. of dark-green tenacious fluid; no calculi. Upon section of the organ dilatation of the veins is seen, especially in the inferior portion of the right lobe. A mottled appearance is also present; this mottling consists of dark-red and lighter areas, resembling the picture usually observed in a nutmeg liver. Weight, 1250 gms. The pancreas, upon section, is slightly hyperemic, but no gross changes are observed. Weight, 100 gms. Stomach and intestines normal. External and internal genital organs are normal.

In the mediastinum in the middle line a large globular mass is seen. It is firm in consistence and covered by a distinct membrane. It extends from the second to the sixth costal cartilage, immediately posterior to the sternum, 3 cm. to the right and 3 cm. to the left of this bone. It is anterior to the trachea, which, with the bronchi, is distinctly flattened. The mass measures from superior to inferior margin 15 cm., transversely 13 cm., and antero-posteriorly 12 cm. Upon incising the sac it is seen to be completely filled with laminated clots too closely allied to enumerate. Upon examining the mass more closely it is seen to be an aneurysmal dilatation of the aorta. This vessel shows dilatation from its origin, the ectasia involving the ascending, transverse, and part of the descending portion of the arch. It is quite markedly atheromatous. Upon the right side the innominate artery comes off from the superior margin of the mass anteriorly to the right of the trachea. Upon the left side the carotid and subclavian arteries come off from the aorta beyond the aneurysm. The superior vena cava traverses the right lateral surface of the mass. The pulmonary artery is posterior and to the left of the mass, and is flattened as a result of the pressure to which it has been subjected.

March 13, 1902.

Streptococcus Mucosus (Howard) and its Relation to Micrococcus Lanceolatus.

WARFIELD T. LONGCOPE, M.D.

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From a brief review of the morphology, biology, and pathogenicity of *Micrococcus lanceolatus*, based principally on Kruse and Pansini's work, it is seen that the organism varies in many particulars from the fixed type. Owing to this fact, several observers have described certain organisms which differed slightly from pneumococcus as distinct species. These, however, were later proven to be forms of pneumococcus. Among these variations should probably be placed the *Streptococcus mucosus* group, recently described by Howard and Perkins; and to establish a close connection between that group and *Streptococcus lanceolatus* the following three cases are recorded: In all three cases the organism resembled the descriptions of Howard and Perkins so closely that they were immediately identified with *Streptococcus mucosus.* In the first case the organism was obtained from a subacute fibrinopurulent pericarditis and an abscess in the left chest-wall which communicated indirectly with the pericardium; in the second case from the pus of an acute otitis media following typhoid fever; in the third case from the circulating blood before death, the heart's blood after death, and consolidated lung of a man who died of typical lobar pneumonia developing during the course of an acute lymphatic leukemia. In the last case the organisms from the circulating blood and heart's blood both presented immediately the characteristic features of *Streptococcus mucosus*, whereas the organism from the lung grew at first in accordance with pneumococcus, but after two to three generations on blood-serum, assumed completely the character of *Streptococcus mucosus.*

From these observations the conclusions are drawn that *Micrococcus lanceolatus* admits of a somewhat wide range of growth from the common type; that these variations may occur as such in a certain number of pathologic lesions; and, finally, that they cannot be considered as definite species, but should be looked upon as transient varieties from the fixed type, their altered characters probably depending upon the peculiar conditions under which they develop. *November* 14, 1901.

Primary Carcinoma of the Liver.

H. D. JUMP, M.D.,

AND

J. D. STEELE, M.D.

The patient, a woman aged seventy-three years, had had yellow fever, bronchitis, endometritis, and influenza. On the 8th of March, 1901, she had a mild attack of biliary colic, which was followed in a week by a second one. After these attacks she was weak and very much depressed in spirits; there was a constant distress in the right hypochondrium, which was at times referred to the right shoulder; the area of liver dulness was not increased, the gall-bladder could not be palpated, and there was no jaundice. On the 20th of April, six weeks later, the inferior border of the liver could be easily felt. From that time her strength failed, and the liver continued to grow until it reached nearly to the crest of the ilium. It was uniformly enlarged and tender and its surface was nodular. The spleen was not enlarged, nor was a growth found in any other organ. She lost very little weight, and at no time in the course of her disease did she become jaundiced. Just before death the legs became swollen, but there was no ascites. The patient died in coma on the 1st of June, three months after the first attack of colic. It is interesting to note that the patient had never had any disorder of the liver previous to this attack and that the beginning of the growth of the carcinoma was coincident with the attack of gallstone colic.

Autopsy. The body was well nourished and rather fat, with very thick abdominal walls. There were some bloody effusions into the peritoneal cavity, with much recent peritonitis about the liver, and with a lesser amount in the lower half of the abdomen. The intestines were free. The liver was tremendously infiltrated by cancerous masses, especially affecting the left lobe. The organ was considerably enlarged and extended as far downward as the umbilicus. The gall-bladder was long, but was not distended, and probably could not have been felt below the edge of the liver. It was filled with large faceted gallstones. The ducts were patulous, and nowhere showed malignant disease. The retroperitoneal glands were not enlarged. The pancreas, spleen, and suprarenal capsules were congested, but not diseased. The kidneys were congested and slightly fatty. The heart showed some stenosis of the mitral valve, with some dilatation and hypertrophy of the right and left ventricles. The uterus showed no malignant disease. There were two small submucous uterine fibromas. A thorough search of the thoracic and abdominal cavities showed no evidence of cancer except in the liver. A microscopic examination of the liver showed that the infiltrating growth was a true glandular cancer. *January* 23, 1902.

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The Lesions in a Series of Eyes which Produced Various Types of So-called Sympathetic Disturbance in the Fellow Eye.

G. E. de SCHWEINITZ, M.D.,

AND

E. A. SHUMWAY, M.D.

To an affection in which one eye is implicated as a result of disease or injury to the other, the somewhat unfortunate term "sympathetic" is usually applied, and two chief classes of this affection are recognized, namely, so-called sympathetic irritation and sympathetic inflammation, or ophthalmitis. They represent two essentially different processes. The present paper deals with the lesions found in a series of eyes which produced sympathetic irritation, in contradistinction from sympathetic inflammation.

Case I. *Nontraumatic iridochoroiditis of the right eye, of uncertain etiology; seven months later sympathetic irritation of the left eye; enucleation; rapid disappearance of the symptoms in the sympathizing eye.*

Clinical History. A married woman, aged forty-five years, in August, 1897, began to notice muscæ before the right eye. In

November iritis was evident, and the usual treatment for that disease was ordered by her attending physician, with negative results. The usual constitutional causes for iritis were absent. There was a doubtful etiologic relationship of influenza. The menopause and its phenomena may have been responsible for the original iritis. When examined by Dr. de Schweinitz, in April, 1898, the right eye was in a state of intense iridocyclitis, the lower half of the cornea was opaque, there was hemorrhage in the anterior chamber, the iris was thickened and infiltrated and covered with yellowish masses; vision, doubtful light perception. The optic nerve of the right eye was hyperemic; there was passive congestion of the retinal veins and slight edema of the fiber layer. Photophobia, imperfect accommodation, and ciliary tenderness were present. The inflamed eye was enucleated, inasmuch as it was intensely painful and practically blind. Operation was followed by a prompt disappearance of all irritative symptoms.

Examination of the Eyeball. The episcleral tissues are infiltrated with round cells, which are collected especially around the dilated bloodvessels. The cornea is entirely normal. The iris is thickened to twice its normal size, and is densely infiltrated with round cells. The anterior chamber is filled with a homogeneous exudate, which contains a few cells; they are more numerous in the angle, which is obliterated by them. Descemet's membrane is, however, intact. The posterior surface of the iris is bound to the lens capsule by an organized exudate. This cellular exudate involves also the ciliary bodies, and extends into the vitreous and surrounds the lens. It is composed of small cells of mononuclear variety, which stain well and show no areas of degeneration. Very few polymorphonuclear cells can be seen, and no epithelioid cells nor giant cells. They are mixed with a large amount of fibrin, but there has been very little attempt at organization of the exudate, except between the iris and lens. In other words, the process is of a distinctly plastic, nonpurulent type, which shows no characteristics of tuberculosis. The lens fibers are beginning to split and show degenerative changes. Anteriorly the choroid shows a moderate infiltration, but posteriorly the membrane is much more extensively involved, especially near the optic nerve entrance. Here it is thickened to many times its normal dimensions by a dense mass of the mononuclear cells, which have broken through the lamina vitrea and extend into the subretinal space. The retina is detached throughout, and shows a similar slight infiltration in its anterior portion, while at the nerve entrance its structure is entirely destroyed and it is embedded in a mass of exudate. The head of the nerve is infiltrated and the round cells extend backward along the septa and form thick mantles around the central vessels.

Diagnosis. Plastic iridocyclitis and chorioretinitis; degeneration of the retina; infiltration of the vitreous; optic neuritis.

CASE II. *Penetrating injury of the inner corneoscleral region of the right eye and traumatic cataract; quiescent for twenty-eight years; then iridocyclitis and recurring hyphemia following a concussion injury; two weeks later sharp sympathetic irritation of the left eye; enucleation of the excitor, followed by prompt subsidence of the symptoms in the sympathizer.*

Clinical History. A man, aged thirty-six years, when eight years old was cut with a piece of china in the right eye, the incision passing in a curved manner through the inner corneoscleral region and somewhat vertically downward and outward across the cornea, incising the lens and deeper structures. Treatment at that time saved the eyeball, which, except for faint light perception, was sightless. No difficulty with the opposite eye was ever experienced, this organ being normal in all respects, until twenty-eight years later, when the patient received a blow on the blind eye with a gloved hand, followed a few hours later by intense pain, deep ciliary injection, and hemorrhage into the anterior chamber. In spite of treatment the cyclitis deepened, fresh hemorrhages occurred, and on the twelfth day after the injury signs of sympathetic trouble were manifested in the opposite eye, namely, photophobia, temporary obscurations of vision, and slight retinal irritability. The injured eye was enucleated by Dr. de Schweinitz, and all sympathetic phenomena promptly disappeared.

Examination of the Eyeball. On the nasal side the iris is drawn into a perforation in cornea, and is adherent on this side to the posterior surface of the cornea back to the ciliary attachment. The cornea is infiltrated, especially on this side. Bowman's membrane is interrupted, and the cap of the iris is covered by scar tissue. The epithelium is degenerated throughout, but separated from Bowman's membrane by a round-cell infiltration. Some of the leukocytes can be seen within the epithelial layers. The iris is infiltrated and atrophic on the nasal side. The ciliary body is hemorrhagic, hyperemic, infiltrated, and pressed flat against the sclera. The lens is cataractous, its capsule is ruptured, and there is some infiltration with lime salts. There is an organized exudate in two masses in the choroid, which is hyperemic. The retina is detached, disorganized, and infiltrated with round cells. The vitreous is shrunken, infiltrated with polymorphonuclear leukocytes and round cells and blood. The infiltrating cells are not in dense masses, and do not show much degeneration (not panophthalmitis). Many of the cells have absorbed blood pigment. The nerve is slightly excavated and atrophied, the nerve sheaths being broken down and showing loss of continuity.

Diagnosis. Iridocyclitis following corneal wound; hemorrhage in the ciliary bodies; detachment of retina; atrophy of nerve.

CASE III. *Traumatic iridocyclitis following a blow on the left eye, which was submitted to some operation, probably removal of a cataractous lens; three months later moderate sympathetic irritation of the right eye, which disappeared on removal of the injured organ.*

Clinical History. A man, aged fifty-six years, was admitted to the wards of the Philadelphia Hospital on November 26, 1901, with the following history: On August 8, 1901, he was struck on the left eye with a fist armed with a false knuckle. Two days later he was taken to the University Hospital, and there some operation was performed, probably removal of the crystalline lens. When admitted to the Philadelphia Hospital the injured eye, in addition to the signs of iridocyclitis, showed a densely hazy cornea, which was infiltrated in almost its entire extent.

The right eye dreaded the light, was slightly tender on palpation, and exhibited a moderate amount of epiphora. Enucleation of the injured eye by Dr. de Schweinitz was followed by a subsidence of the irritative phenomena of the opposite eye.

Examination of the Eyeball. The epithelium of the cornea is irregular; Bowman's membrane dips in in several places, and is separated from the epithelium in one place by round cells. The cornea shows vessel formation and some infiltration with cells. The episcleral tissues are thickened and infiltrated; the vessels hyperemic. The scar from the incision extends through the cornea above. The iris is healed to posterior surface of the cornea here, and Descemet's membrane is interrupted. A dense organized membrane extends from the inner surface of the wound along the anterior surface of the iris stump to the opposite border of the pupil. Descemet's membrane has pulled loose from the cornea and is adherent to it. The iris is atrophic from the old iritis; clumps of pigment are scattered through dense stroma; the vessels are thickened and obliterated. The opposite side of the iris is pulled out and very atrophic, nothing but pigment remaining in places. There is a granular exudate in the anterior chamber. The ciliary bodies are quite atrophic, the muscle fibers have disappeared; the ciliary processes have undergone advanced hyaline change and the vessels are obliterated. A thin membrane containing a few cells extends back of the iris into the vitreous. There is no trace of lens or capsule; there is advanced chorioretinal atrophy. The nerve is atrophic, quite narrow, and shows overgrowth of septa.

Diagnosis. Iridocyclitis following traumatism; advanced chorioretinitis with optic-nerve atrophy.

CASE IV. *Cyclitis of the right eye following foreign body in vitreous (piece of copper); foreign body removed; eye moderately quiescent for eight months, then renewed cyclitis with hemorrhages into the anterior chamber; sympathetic irritation of the left eye; prompt disappearance of sympathetic symptoms after enucleation.*

Clinical History. A boy, aged thirteen years, in July, 1898, was struck in the right eye with a piece of copper cap, which, on October 7, 1898, Dr. Hansell removed from the vitreous. In three weeks the patient was discharged, with the injured eye in good condition. The opposite eye had at this time shown no signs of disturbance. He was not seen again until May 5, 1899, when he reappeared with marked cyclitis and the anterior chamber filled with blood. The left eye showed marked signs of sympathetic irritation. The injured eye was enucleated by Dr. de Schweinitz, and the operation followed by complete subsidence of the irritative phenomena in the opposite eye.

Examination of the Eyeball. The corneal epithelium and Bowman's membrane are intact; the substantia propria shows a few vessels and a large quantity of blood pigment between the lamellæ in fine yellow granules. The anterior chamber is full of old blood extravasation; the cells on Descemet's membrane show blood pigment in clumps. There is a dense organized membrane on the surface of the iris twice the thickness of the iris at its center. The iris shows condensation of tissue, round-cell infiltration, thickening of vessel walls, endarteritis, destruction of stroma cells, with clumping of pigment. Adherent to the cornea at its periphery is a dense exudate posterior to the iris, into which the ciliary processes have been drawn. The lens is absent; there is a trace of capsule. The retina is detached, disorganized, lying in the center of the vitreous and extending from the nerve entrance to mass of exudate back of the iris. The vitreous shows several large hemorrhages. All tissues are blood-infiltrated, with large pigment clumps everywhere. The ciliary bodies show considerable organized tissue. The choroid is thickened posteriorly and the vessel walls are thickened. The nerve is infiltrated, partially atrophied. The sections stained with HCl and potassium ferrocyanid did not give iron reaction.

Diagnosis. Old iridocyclitis; intraocular hemorrhages, new and old; partial nerve atrophy; disorganization of retina.

CASE V. *Iridocyclitis of the left eye caused by a penetrating wound of the lower ciliary region, made with a pointed stick; one month later marked sympathetic irritation of the right eye; gradual disappearance of the sympathetic phenomena after enucleation.*

Clinical History. A boy, aged ten years, on the evening of July 6, 1901, was struck with a wooden splinter in the left eye, which penetrated the ciliary body and caused a prolapse of the ciliary tissue into the wound. The patient was not seen until about twenty hours after the accident, when the prolapsed tissue was removed. For sixty hours the eye did well; then, however, iritis set in, and gradually iridocyclitis, with the formation of a perfectly visible exudate posterior to the lens. All treatment was unsuccessful in subduing the inflammation. One month after injury muscæ began to appear before the right eye, which for two days previously had exhibited some photophobia. No fundus lesions, except marked overfilling of the retinal veins, were evident, but loup examination of the cornea indicated slight edema of the corneal endothelium. The fluorescin test, however, was not applied. After enucleation by Dr. de Schweinitz these symptoms gradually disappeared, although they were still manifest for about two months. At the present time vision is normal.

Examination of the Eyeball. The episcleral tissues are moderately thickened, the vessels are full and surrounded with round cells. The cornea, especially at the limbus and Schlemm's canal, shows numerous round cells. The anterior chamber contains a homogeneous exudate filling the angles and extending across the surface of the iris and in the pupillary area; a few polynuclear cells are entangled. The iris and ciliary bodies show round cells scattered through their stroma; these are especially grouped around the bloodvessels and are mostly mononuclear cells. The bloodvessels are full and contain many polynuclear leukocytes. The pigment has been pulled away from the posterior surface in one position and is adherent to the lens capsule. The anterior layers of the cortex are separating and show beginning collections of fluid between. Posterior to the lens is a well-formed membrane, composed of organized tissue containing capillary bloodvessels. The posterior layer of this membrane is fresh exudate and contains loose-meshed fibrin and many round cells, chiefly mononuclear, which have not yet organized. The membrane extends on to the ciliary processes and the round-cell exudate may be traced on to the retina. The retina is artificially detached and shows on its surface collections of round cells, particularly over the vessels. The vessels contain polynuclear cells and are surrounded by thick mantles of mononuclear cells, partly within and partly broken through the perivascular lymph sheaths. This infiltration surrounds also the central vessels. Posterior to the lamina the nerve is normal; the retina is edematous and shows diffuse infiltration, with round cells.

Diagnosis. Iridocyclitis following wound of ciliary body.

CASE VI. *Cataract extraction, left eye, followed thirteen days after extraction by infection, manifesting itself in the form of a recurring hypopyon and iritis, the infection apparently due to a pneumococcus conjunctivitis then prevalent; distinct sympathetic irritation of the* *right eye three months later, relieved entirely by enucleation of the excitor.*

Clinical History. A man, aged thirty-eight years, was admitted to the wards of the Philadelphia Hospital with a cataract of the left eye, which, after preliminary iridectomy, was removed by one of the attending surgeons on July 23, 1900. Healing was smooth, and all did well until the thirteenth day, when the eye was attacked with conjunctivitis of the pneumococcus variety. It is supposed that from this source the infection passed through the not firmly healed operation wound and the iris became infected. Hypopyon was soon manifest, and was several times evacuated, but the eye remained in a condition of iridocyclitis, which was very marked when Dr. de Schweinitz took charge of the wards on October 1st. In addition to the iritis and cyclitis, the cornea was markedly vascularized and showed below thickened scar tissue at the point where the incision to relieve the hypopyon had been made. The right eye exhibited marked signs of sympathetic irritation. The left eye was enucleated by Dr. de Schweinitz on October 13th, to the man's immediate relief.

Examination of the Eyeball. The cornea shows well the position of the incision above filled in with scar tissue, and the corresponding section of Descemet's membrane into which stump of iris is healed. The upper half of the cornea shows absence of Bowman's membrane and irregularity of the lamina beneath, with new vessels and round cells. The episcleral tissues are edematous, infiltrated, and hyperemic. Bowman's membrane is intact over the lower half of the cornea, and the laminæ are more regular, but are infiltrated and show new vessels. From the inner surface of the incision a band of organized exudate extends inward and backward, and the iris on the opposite side is drawn over into it. The iris shows old iritis, round-cell infiltration, organization of tissue, destruction of pigment cells, and old hemorrhages. The exudate behind the iris is partly organized and contains old blood extravasations, lens capsules, and a small amount of lens cortex. The ciliary processes are drawn inward; the retina is partly detached, with small amount of subretinal homogeneous exudate. The retina is edematous; Müller fibers quite prominent. There is perivasculitis, and the head of the nerve and surrounding tissue are swollen.

The central vessels are distended, the nerve and fiber layer moderately infiltrated. The nerve fibers stain fairly well; the choroid is normal; the vitreous shows moderate round-cell infiltration; no microorganisms could be found in the anterior part of the eyeball.

Diagnosis. Iridocyclitis following cataract extraction.

CASE VII. *Cataract extraction, right eye, followed by iridotomy; two months later iridocyclitis of this eye and plastic iritis of the opposite eye; exciting eye enucleated; uncertain outcome of the disease in the opposite eye; patient syphilitic.*

Clinical History. A man, aged sixty years, was admitted to the Jefferson Medical College Hospital for the operation of cataract extraction. The operation and also capsulotomy were successfully performed by Dr. Hansell, but were followed by some iritis. The patient was dismissed when the eye was quiet, and, although cautioned to return, he did not put in an appearance for nearly two months later, when he appeared with the eye on which the two operations had been performed in a state of iridocyclitis, and with distinct although moderately produced iritis upon the opposite side. After consultation with Dr. Hansell, Dr. de Schweinitz enucleated the right eye and placed the patient on treatment for the left eye, particularly large doses of mercury and iodid of potassium. Recovery from the enucleation was uneventful and the iritis somewhat improved. The patient was dismissed from the wards to attend the dispensary, but drifted away, and was not seen again.

Examination of Sections of the Eyeball. There is a scar in ciliary region into which the iris is drawn, so that the cicatricial tissue contains much pigment. The cornea is normal except for the scar. Descemet's membrane is ruptured and curled up. The episcleral tissues are infiltrated with small mononuclear cells. The iris is covered on its anterior and posterior surfaces by organized and organizing exudate. Much of it is recent and contains cells with deeply staining nuclei surrounded by considerable protoplasm, and are evidently fibroblasts. No trace of the lens is present, except the capsule folded up in the exudate. The iris is densely infiltrated with round cells, and has lost very largely its normal structure; it is adherent in many of the sections to almost the entire length of the posterior surface of the cornea through the medium of the exudate. The ciliary bodies are infiltrated, the choroid likewise. The retina is probably artificially detached. It is edematous, its inner surface covered with a nearly uniform layer of fibroblastic cells, and it contains in addition many round cells; these are grouped especially about the vessels. Many of the latter are obliterated; nearly all show wide distention of perivascular lymph sheaths and dense infiltration of the space thus produced. The endothelium is extensively proliferated; the rods and cones are in fair condition; the vitreous shows membranes of fibrin meshes containing round cells. The nerve head is infiltrated, like the retina, with round cells, especially around the small vessels and in the intervaginal sheath. The central vessel contains a number of polymorphonuclear cells. The nerve fibers are normal; the ganglion cells of the retina have lost their granules, and many of them show minute vesicles in the protoplasm.

Diagnosis. Iridocyclitis after cataract extraction in a syphilitic patient; perivasculitis retinæ.

CASE VIII. *Iridocyclitis of right eye following cataract extraction; sympathetic irritation of the other eye, which rapidly disappeared after enucleation of the excitor.*

Clinical History. A man, aged about sixty years, was admitted in November, 1899, to the wards of the Philadelphia Hospital with well-marked iridocyclitis of the right eye, from which a cataract had been removed at another hospital, from which he was dismissed when the eye appeared to be quiet. Prior to the operation the eye had been highly myopic. He had probably suffered from the iridocyclitis for about two months. The inflamed eye was enucleated by Dr. de Schweinitz, and there was prompt subsidence of a decided sympathetic irritation in the opposite eye, on which also an operation for cataract had been performed.

Examination of the Eyeball. The tunics are very much thinned, especially in the posterior half. The cornea is wrinkled, shows absence of Bowman's membrane, and exhibits new vessel formation and round-cell infiltration. There is a scar above from a former cataract incision, with infiltration of its edges, and Descemet's membrane is curled up at this point. There is an old plastic iridocyclitis with membrane formation which extends from the corneal wound across the surface of the stump of the iris to the opposite border of the iris. The iris is very much thickened by mononuclear round cells, and its vessels are hyperemic. The ciliary processes are drawn into the organizing exudate. Back of the iris the mass includes the lens capsule, the lining cells of which are proliferated. There is a small amount of swollen cortex of the lens remaining. The choroid is moderately infiltrated with mononuclear round cells. The retina is folded up in the center of the vitreous; it is disorganized, and shows a few infiltrated round cells, especially around the vessels. The nerve is normal; the sclera is very much thinned.

Diagnosis. Plastic iridocyclitis following cataract extraction; detachment and degeneration of the retina.

In these eight cases, with one exception, there is iridocyclitis following traumatism or operative interference. This inflammatory process is not purulent, but plastic in type, and is accompanied by considerable fibrin formation. When it has lasted a sufficiently long time there is organization of the exudate and membrane formation. In two of the eyes there has been hemorrhage from the vessels of the ciliary bodies. In all the eyes except one there are marked choroidal lesions; infiltration with round cells in five; hyperemia and blood extravasation in one; atrophy in one. Four eyes show perivasculitis in the retina and nerve, and in two the process is so intense as to form dense mantles of cells in the perivascular lymph sheaths, which are plainly visible macroscopically in one of the specimens. In other words, the lesions are those which one expects to find in eyes which have produced the so-called sympathetic ophthalmitis—that is to say, which have produced an inflammation in the other eye resembling in its clinical and pathologic features the inflammation in the eye which excited it, and yet with the single exception of one case, the patient being syphilitic, and the iritis, therefore, possibly of this nature, the so-called sympathetic disease manifested itself as an irritation and was subdued by the removal of the exciting eye.

It is not germane to the present paper, which is intended only to describe these specimens in connection with their exhibition, to discuss the theories of sympathetic ophthalmitis. It is enough to say that the old hypothesis that the disease was due to a reflex action through the ciliary nerves has largely been abandoned for the theory of infection. The migratory theory developed by Deutschmann, according to which such an inflammation is of bacterial origin, and is to be explained by a progressive process in the continuity of the tissue of one eye to the other by way of the optic nerve apparatus, has not been confirmed by other observers; so much so, that even so clever an investigator as Greeff has said the migratory theory is still a hypothesis, just as is the ciliary nerve theory. To be sure, those who have failed to confirm Deutschmann's conclusions are unwilling to deny the bacterial origin of the disease, but neither the micro-organisms nor the route of transmission has been discovered with certainty. It is possible that future investigations will confirm a recent theory that not the microorganisms but their metabolic products are the etiologic factors in these cases, or, in other words, that a toxin is liberated by them which acts as the exciting agent.

Sympathetic irritation is a totally different manifestation, which apparently is a neurosis in some instances. It has been believed, and is still advocated, that the pathway of the impulses which produce sympathetic irritation is composed of the short ciliary nerves which come from the ciliary ganglion and of the nerves which enter into the composition of this structure, namely, the nasal branch of the ophthalmic, the third nerve, and the sympathetic. Among these, according to Randolph, the nerves which have most to do with the sympathetic irritation are the fibers derived from the fifth and the sympathetic. It should be remembered that sympathetic irritation, although it may be a forerunner of sympathetic ophthalmitis, is by no means necessarily so, and in our experience not ordinarily so. In other words, sympathetic irritation is promptly cured by removal of the excitor, and disappears without leaving structural changes. It may last for years and appear and reappear in the form of attacks of irritation.

The interesting question is why should a series of eyes such as we have presented this evening, which exhibit typical lesions in the ciliary body and choroid ordinarily concerned with sympathetic ophthalmitis, produce sympathetic irritation only, one case being excepted, and that somewhat doubtfully. The answer may be that in all of these cases the enucleation was performed with sufficient promptness to check sympathetic ophthalmitis. This cannot well be the case, for in some instances an iridocyclitis had lasted for long periods of time, long enough, in other words, if there were no other factors at work, to have produced the inflammation and not only the irritation. It is conceivable that one patient suffering from plastic iridocyclitis the result of injury will beget a sympathetic ophthalmitis in the other eye because the resisting force of that organ is deteriorated. In other words, it would seem to us very important that in these cases the widest general examination of the patient should be made to determine the possibility of general conditions which might be predisposing factors to such an inflammation. It is Panas, we think, who believes that these cases of sympathetic ophthalmitis furnish examples of autoinfection, not in the sense of a migratory ophthalmitis, but, as Hubbell has said, " in the sense that the uveal tract of the sound eye, by reason of a lowering of its vital tone through the extreme reflex and vasomotor disturbances, kept up by a foreign body in or injury to the other eye, becomes truly poisoned or infected by materials in the general circulation to the extent of inducing a most obstinate and uncontrollable inflammation."

It will be seen that here also these observers do not entirely escape from the reflex theory, or sympathetic theory, which in our day of pathologic research does not seem to be a scientific one.

The best that can be said at the present time is that an eye so wounded that a plastic iridocyclitis or uveitis appears sometimes sets up in the opposite eye an analogous inflammation, to which we give the name sympathetic ophthalmitis, and that in all probability this depends upon an infection of the so-called sympathizing eye by some form of bacteria or some form of toxin which they liberate, but that sometimes exactly analogous lesions will produce only an irritation which promptly disappears on removal of the originally injured eye, and disappears, moreover, without leaving a trace of organic change, and that it would further seem that some undiscovered, perhaps constitutional, perhaps local, condition determines on the one hand the inflammation and on the other hand the temporary so-called irritation.

March 13, 1902.

Diagnosis by Means of the Formed Elements of the Blood.

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The title of my paper (which was suggested by the Business Committee) suggests for discussion the four following subjects:

1. The absolute diagnosis of disease by means of the formed elements of the blood.

2. The analysis of the blood as a part of a thorough examination of a patient.

3. The thoroughness of the blood examination. It should not be simply the estimation of the hemoglobin and the enumeration of the corpuscles, but it should also include a thorough morphologic study, and, where indications are present, a complete chemical and bacteriologic analysis.

4. The consideration of such a thorough examination, in connection with the complete history of the case, with the duration of the disease, with the results of other clinical methods, and with possible complications.

1. I know of no disease that can be diagnosed absolutely by means of the formed elements of the blood. Even in malaria the diagnosis depends upon the finding of the parasite which infects the erythrocyte. Likewise, not to be included in this statement, are the extracorpuscular parasites found in relapsing fever and in filariasis. An apparent exception to this statement is presented by leukemia. The blood picture in a typical case of splenomyelogenous leukemia, with a high corpuscular (leukocytic) count, a high percentage of myelocytes, and a marked degeneration of the erythrocytes is scarcely to be mistaken for any other disease. In lymphatic leukemia, however, one is not as sure of the diagnosis as one is in the mixed (splenomyelogenous) form of the disease, when a high count of the leukocytes is present, as other conditions may show similar blood changes. Cases of sarcoma have presented blood pictures identical with those of lymphatic leukemia, and the lymphocytosis found in pertussis (Frölich and Meunier) and in pneumonia of children (Cabot) is at times difficult to distinguish from this form of leukemia with low leukocytic counts. Furthermore, in both forms of leukemia—splenomyelogenous or

lymphatic—an intercurrent disease may so alter the blood picture, by changing the type of the leukocytosis, by causing the number of leukocytes to be reduced within normal numbers, or by changing the blood so that it suggests a simple secondary anemia that the usual pictures in these diseases are entirely lost.

The intercurrent diseases reported as producing this change are: Typhoid fever (Eisenlohr), miliary tuberculosis (Quincke), chronic tuberculosis (Stintzing), icterus (Mosler), erysipelas (Freudenstein), purulent pleuritis (a later complication of articular rheumatism gave no change, Heuck), sepsis (Frölich, Müller, Fränkel, Cabot), influenza (Kovacs), pneumonia (Thorsch), "tubercular infection" (Zappert, Lichtheim). Here may also be included the effects of drugs upon the blood findings in a number of typical cases of leukemia. Taylor and McCrea report cases—the former three and the latter one—in which the therapeutic action of arsenic, even after relapses, brought the blood back to nearly a normal condition. The splenic tumor in these cases did not disappear as the blood picture returned to normal. Osler, Stengel, and Rensselaer report similar cases.

Strattmann and Huesner each report a case of leukemia in which the abdomen was opened, the blood picture afterward returning to normal. In the latter's case a relapse is recorded. Further, the picture of leukemia has changed in the ante-mortem stages of the disease, the change here being probably due to terminal infections or to circulatory disturbances.

2. That the examination of the blood is an essential and valuable part of a thorough examination of a patient needs no comment. Careful and thorough clinicians, medical men or surgeons have long since learned the importance of blood examinations. Such general expressions about the blood as "of scientific, but often of no practical value, and may misguide the surgeon" only show that the authors of such statements have a very, very limited knowledge of the subject upon which they attempt to write, or that they seek one sign alone upon which to make their diagnosis, and failing, as they have undoubtedly failed, they now condemn entirely the value of blood examinations. On the other hand, the man who makes all his diagnoses from the cover-glass preparation alone—*i. e.*, scarlet fever, obscure sarcoma, and the like, and who

distinguishes bacteria in this way—will inevitably make as many mistakes as his colleagues who do not know the value of that which they condemn.

3. The blood analysis should be a thorough one. This is a rule which is, unfortunately, too often overlooked. Attracted by the apparently simple technic of blood examinations, many have sought this field with the idea that corpuscular counts and estimation of the hemoglobin would make a diagnosis easy and rapid. The numerous tables of corpuscular counts, which have been compiled to convince the profession that in certain diseased conditions the corpuscles should be found in definite numbers per cubic millimeter, have surely failed their purpose. Thus it will be seen from Cabot's tabulated counts of seventy-two cases of appendicitis, that Case I. showed 52,000, and Case LVII. 9000 leukocytes per cubic millimeter; both cases showed pus at the time of the operation. In the purulent cases reported by Da Costa one showed a leukocytosis above 50,000 cells per cubic millimeter, while in seven other purulent cases the leukocytic count varied between 5000 and 10,000 per cubic millimeter. These counts represented practically the same pathologic condition at the time of the operation—appendicitis, with abscess formation—and yet the leukocytic counts varied between very wide margins.

That the formed elements of the blood should be studied from their morphologic stand-point, as well as from the number of corpuscles per cubic millimeter, is well attested by comparing those diseases which, from a clinical stand-point, are at times difficult to separate. Time will not allow a complete analysis or comparison of all these diseases; therefore only the most important will here be considered.

The so-called Essential Progressive Pernicious Anemia *versus* Carcinoma. From the clinical stand-point these conditions may not be distinguished by the physical signs and the symptoms they present, nor can they be distinguished in some cases after the usual blood examination of corpuscular counts and hemoglobin value. Yet, as a rule, cases of progressive pernicious anemia have a very low erythrocytic count when they first come under observation. This count is usually in the neighborhood of 2,000,000 cells per cubic millimeter. The leukocytes per cubic millimeter are normal or their number is slightly below the normal figures. The total amount of the hemoglobin of the blood is reduced, often to a very marked degree. However, this reduction in the coloring matter is rarely as great as it is in other conditions with equal corpuscular counts. On the other hand, in the majority of cases of this disease an increased richness of hemoglobin per cell is to be found; this increase may reach to twice as much per cell as is found under normal conditions. In 183 cases collected from various authors of this disease 72 per cent. showed an increased corpuscular richness in hemoglobin. Color index in these cases averaged 1.19.

In carcinoma, as a rule, the erythrocytic count is rarely low when the case is first observed, and even in advanced cases with severe cachexia the counts seldom fall below 1,000,000 cells per cubic millimeter. The leukocytes may vary in number per cubic millimeter, according to the size, location, and the rapidity of the growth. When the erythrocytic count is very low the leukocytic count almost invariably shows an increase (Cabot). However, cases of carcinoma may show, as stated above, the same results in the estimations of corpuscular counts and hemoglobin as cases of progressive pernicious anemia. When the counts and the hemoglobin value are not suggestive of either disease the study of the morphologic changes in the cover-glass preparation may add very much to distinguish the two diseases.

Progressive Pernicious Anemia. Marked erythrocytic degeneration is an early and constant finding in cases of progressive pernicious anemia. Poikilocytosis—an irregularity in the shape of the cell—is a degeneration which is seen early in the disease, and very soon becomes marked in the progress of the case. Anisocytosis—an irregularity in the size of the cell—is noted early, the macrocytes or the larger cells, as a rule, predominate. Polychromatophilia—a condition where the erythrocytes stain homogeneously with a combination of several stains—is invariably to be found, and it usually accompanies the enlargement of the cell. Basic granulation, or granular degeneration of the erythrocyte, is almost always found. These degenerated cells may be very numerous; in some severe cases the number may be equal to the excessive numbers found in chronic lead poisoning. The smaller cells—the microcytes—may show an unusual depth of staining power with the acid stain. Nucleated erythrocytes—erythroblasts—are always present in the peripheral circulation; often they are very numerous, and all types are to be seen—normoblasts, macroblasts, microblasts. Macroblasts almost invariably predominate; these cells are rarely to be seen predominating in conditions simulating this disease, except in bothriocephalus anemia. Karyokinesis is rarely seen in these larger cells; if found with the above blood picture it forms almost a pathognomonic finding of progressive pernicious anemia.

The corpuscular richness in hemoglobin, as stated above, is, in the majority of cases, increased; this is seen histologically by the deeper staining of the cells than is normal. Many of the cells are larger and flatter, and therefore contain more coloring matter. The flatness is due to the fact that the biconcavity is lessened or entirely absent in many of the cells.

The leukocytes may be present in normal numbers, or as usually the case, a leukopenia—a decreased number of leukocytes per cubic millimeter—is found. The reduction in the number of leukocytes is usually due to a decrease in the polymorphonuclear leukocytes; consequently, a relative lymphocytosis is the rule. Schreiber has noted an increased number in the divisions of the nucleus of the polymorphonuclear cells, which, he suggests, is characteristic of the disease. This can scarcely be accepted, as other conditions—sepsis, so-called splenic anemia, and carcinoma—may show the same condition of the nucleus.

Carcinoma. In this disease rarely are the degenerative changes in the erythrocytes, as above noted, in such evidence. Poikilocytosis is only moderate even in the severe cases, and rarely does it become marked. Anisocytosis is moderate in degree; the microcytes usually outnumber the macrocytes. Granular degeneration and polychromatophilia are to be seen in moderate degrees in the severer cases. Nucleated erythrocytes are almost always present in advanced cases. Normoblasts and macroblasts are found; the latter are, however, infrequent; rarely indeed, if ever, is the larger cell to be found in excess of the normoblasts. Deficiency in hemoglobin is the rule; histologically, this is noted by deficiency in stain and an enlargement in the normally pale central area of the cell.

In this disease a leukocytosis is usually present; however, tumors of slow growth, localized or away from vital parts, may not produce an increase in the leukocytes. In cases where these cells are not increased in numbers the predominance of the polymorphonuclear leukocytes is the rule.

Another instance in which this same difficulty arises is that of chlorosis versus secondary anemias. The distinction between chlorosis, on the one hand, and the numerous conditions which come under the class of secondary anemias, on the other, is frequently very difficult, if the findings of the blood alone are considered. Especially is this true if one is dealing with a slight grade of anemia. In both conditions the corpuscular counts may be the same, and the hemoglobin slightly or only moderately reduced,

Chlorosis. In chlorosis the deficiency in the coloring matter and an undersized condition of the erythrocytes are more or less characteristic, and in moderately severe cases these may be the only abnormal changes in the blood. Usually, however, when there is a great decrease in hemoglobin the erythrocytic count generally falls; rarely, however, below 3,000,000 cells per cubic millimeter. The other degenerative changes in the erythrocyte are not marked. In the severer cases a slight poikilocytosis and a few granular degenerated cells may be found. Nucleated erythrocytes may at times be seen; these are of the normoblastic type. The number of leukocytes per cubic millimeter is generally within normal boundaries. A relative increase in the lymphocytes is usually to be found.

Secondary Anemia. In secondary anemias, which may be produced from various causes, the blood may show a more or less similar picture to chlorosis. The erythrocytes are reduced in numbers, and the degenerations in these cells may be only very slight, or marked, according to severity and to the nature of the cause. The hemoglobin is usually reduced slightly more than the reduction of the erythrocytes. The leukocytes are generally increased in number; this, however, depends upon the cause of the anemia. A normal number of leukocytes, or a normal number with an increase of the polymorphonuclear leukocytes, or a leukopenia, may be found. The difficulty in diagnosis arises only in the pronounced cases, and then the blood picture of a moderately severe case of chlorosis may be seen in cases of secondary anemia from almost any cause.

Toxic Substances. These substances are mentioned here simply because they produce changes which are similar to the changes found in the blood of the primary or secondary anemias mentioned above. The action of toxic substances or of drugs in toxic doses upon the blood has lately received marked attention. These substances produce a pronounced change in the erythrocytic count and distinct degenerative changes in these cells. The action upon the leukocytes—*i. e.*, the production of a leukocytosis or of a leukopenia varies according to the substance or to the class of substances encountered. From the view of hematology, these toxic substances should receive more careful study, both from a clinical as well as from an experimental stand-point, as they will undoubtedly throw some light upon the etiology of some of the obscure anemias.

Some of these substances which have been partially studied are: Snake poisons, poisoning from toadstools, nitrites, guaiacol, nitrobenzol, potassium chlorate, antifebrin, antipyrin, pyrogallol, pyrogallic acid, pyrodin, corrosive sublimate, anilin. All of these have a direct action upon the erythrocytes, causing a marked reduction in their numbers within a very short time after toxic quantities have been ingested. Ehrlich and Lindenthal, in one case of poisoning from nitrobenzol, were able to make a complete study of the blood from a few hours after the drug produced the first symptoms of its toxic action to death. The erythrocytic count fell rapidly to 900,000 cells per cubic millimeter before death on the nineteenth day. All forms of erythrocytic degeneration were noted and became marked early in the course of the case. Nucleated erythrocytes were seen early, and were present in great numbers; all types were seen. The leukocytes varied in numbers; at first there was no increase; later, after the ninth day, a mixed leukocytosis was present, and this was so marked at times that the blood picture was not unlike leukemia.

The effects of lead salts, either as a drug or in leadworkers, have received careful study of late, from the fact that this metal brings out an almost characteristic change—in granular degeneration of the erythrocyte. The usual blood findings in cases of saturnism are a mild chlorotic anemia, with or without a mild leukocytosis. The constant and almost characteristic finding in these cases is the presence of the granular degeneration in the erythrocytes. This peculiar degeneration is seen very early, even before subjective symptoms are noted. (Experimentally within twenty-four hours, after 7.5 grs. were taken.) The number of degenerated cells increases with the severity of the intoxication, and they disappear with the elimination of the metal from the system. This form of degeneration also appears in progressive pernicious anemia, leukemia, and slightly in some other common conditions. However, these conditions rarely present symptoms which might be mistaken for cases of saturnism.

4. Having a complete analysis of the blood, this complete analysis should be considered *only* with the results of the complete clinical findings, the history of the case, the duration of the malady, and the presence of possible complications.

The differential diagnosis between chlorosis and secondary anemia cannot be made absolutely—and it can be suspected only in a very small percentage of cases—from the blood examination alone. But when the blood examination is coupled with the results of other examinations, the history of the case, and the presence or absence of sufficient cause to produce a secondary anemia, the diagnosis becomes comparatively easy. In other words, the diagnosis here must be made by exclusion.

The differential diagnosis between progressive pernicious anemia and carcinoma, especially carcinoma of the stomach, may be approached only from the blood in some cases. And here a *complete* analysis of the blood must be made before the consideration of the blood can be of any value. Cases are observed, however, where a differential diagnosis between these two diseases cannot be made from the blood nor from the blood and clinical findings, nor by any other methods known in medicine today. Fortunately, these cases are rare.

That the results of a complete analysis of the blood should be considered *only* in connection with other complete clinical data applies with no less importance to the class of cases which might be included within the broadest meaning of the term septic infection. The rule in this class of cases is a leukocytosis if the patient is reacting. In slight infections or in severe infections (when the patient is overwhelmed with the products of septic infection and not reacting) no leukocytosis is observed.

Certain well-known facts should be observed in studying the blood in cases of septic infections before the results of a complete blood examination can be of any possible value.

A. That in the earlier stages of an inflammation, when simple engorgement of the vessels and beginning exudation alone are present, as well as in the later stages when pus is found, a leukocytosis is the rule. Exceptions to this rule are infections from typhoid, influenza, tuberculosis, etc. Hence slight catarrhal inflammations as well as phlegmonous conditions may be accompanied by an increase in the number of leukocytes.

B. The degree of the leukocytosis may go hand-in-hand with the severity of the inflammatory process: and this may perhaps be considered a general rule. A much better rule in regard to the degree of leukocytosis is: Every patient is a law unto himself. For example, a small stitch abscess produced 20,000 leukocytes per cubic millimeter in one patient; while in another a general peritonitis from a ruptured tubal abscess, with "quarts of pus," produced 19,000 leukocytes per cubic millimeter. Two cases subjected to the same operation—*i. e.*, ventral suspension and curetment—had practically the same number of leukocytes before operation—*i. e.*, 9760 and 9440 cells per cubic millimeter; each reacted to the operation (postoperative leukocytosis) the first increased to 17,000 and the second to 24,520 leukocytes per cubic millimeter.

C. After the acute or infiltrating stages of the inflammation have subsided the leukocytic count decreases. This is true, whether the exudate is absorbed or walled in—localized. Considering this known fact, the common expression, "I found ounces of pus, and without any indication of it in the blood," scarcely seems warranted.

D. Cases of low leukocytic counts (normal for these patients), counts of 4000 to 5000 cells per cubic millimeter, may show a marked leukocytic reaction to irritation—as an operation—without the increased number of cells exceeding the boundaries of the normal leukocytic count. An increase of over 75 per cent. in the leukocytic count has been observed in this class of cases, the count still coming within normal or practically normal limits. The leukocytic count, or the blood analysis, if considered simply as an estimate of the number of cells per cubic millimeter, is, of course, misleading in this class of cases. If, however, a differential count of the leukocytes were made in such cases, and from it the absolute count of the polymorphonuclear cells determined, an increase of these cells above their normal numbers per cubic millimeter would be of almost as much value as an actual increase in the total number of leukocytes.

Case XXIII. ("Observations of Blood Changes following Celiotomies," *University Medical Magazine*, June, 1900) showed before the operation, which was for a ventral suspension of the uterus: Leukocytes, 4885 per cubic millimeter, and 71.5 per cent. of polymorphonuclear leukocytes, which equalled an absolute count of these cells of 3493 per cubic millimeter. Within five hours after the operation the leukocytic count numbered 8680 cells per cubic millimeter, the polymorphonuclear leukocytes had increased to 81.4 per cent., which equalled an absolute count of these cells of 7066 per cubic millimeter. The reaction in this case of a primary low leukocytic count to the operation was an increase of 3795 cells per cubic millimeter in the total leukocytic count, or a 77.6 per cent. increase in the leukocytes. The polymorphonuclear leukocytes showed a relative increase of 9.9 per cent., or an actual increase of 102.3 per cent., which equalled an increase of these cells to 3573 cells per cubic millimeter as the result of the operation. This case shows the value of a complete analysis of the blood, and at the same time the value of considering the case from the point of view of the surgical intervention in its relation to a leukocytosis. Had a count of this case been made after the operation, and the blood not further studied, it might have been thought that it was an exception to the general rule of a postoperative leukocytosis, *i. e.*, that it had not reacted to a cause that usually produces a leukocytosis.

The polymorphonuclear leukocytes alone may show a relative or an absolute increase, or both, in their number, during the course of a disease or during the convalescence of a patient from a surgical operation, which increase is indicative of alterations in the condition of the patient.

CASE XXIV. (Same series as above.) Operation, ventral suspension of the uterus. The third day after the operation the leukocytic count numbered 12,000 cells per cubic millimeter, polymorphonuclear leukocytes 67.7 per cent., which equalled an absolute count of these cells of 8530 per cubic millimeter. During the night of the third day, after the above count had been taken, the patient developed a slight catarrhal pharyngitis which caused pain on swallowing. The leukocytic count on the next day showed 9000 cells per cubic millimeter; polymorphonuclear leukocytes 73.4 per cent., which equalled an absolute count of 6606 cells per cubic millimeter. In this case the throat condition, which was very slight indeed, caused a relative increase in the polymorphonuclear cells of only 5.7 per cent., while the total number of the leukocytes and the absolute number of the polymorphonuclear cells decreased.

CASE I. (Of the same series.) *Exploratory Celiotomy.* A large tubal abscess was found, but not opened. Before operation the leukocytic count was 12,640 cells per cubic millimeter; polymorphonuclear leukocytes 78.6 per cent., which equalled 9935 cells per cubic millimeter. Within five hours after the operation the leukocytic count was 17,720 cells per cubic millimeter; polymorphonuclear leukocytes were 86.6 per cent., which equalled 15,346 of these cells per cubic millimeter. This count fell gradually for three days to 14,840 leukocytes per cubic millimeter; polymorphonuclear leukocytes 70.0 per cent., which equalled 10,388 of these cells per cubic millimeter. On the fourth day after the primary operation the abscess was aspirated per vagina. In the blood count the reaction to this simple operation was: leukocytes, 10,680 per cubic millimeter, polymorphonuclear leukocytes, 83.1 per cent., which equalled 8875 of these cells per cubic millimeter. Here an actual decrease in the total count of the leukocytes and the polymorphonuclear cells per cubic millimeter, with a relative increase of the latter cells of 13.1 per cent., marked the aspiration of the abscess.

CASE VII. (Of the same series.) The result of the removal of a drain. A comparison of the leukocytic count of the previous day with the count taken immediately after the removal of the abdominal drain showed a decrease of 320 cells per cubic millimeter, a relative increase in the polymorphonuclear leukocytes of 3.3 per cent., and an actual increase of 124 of these cells per cubic millimeter. This case shows practically a stationary condition in the daily count of the leukocytes. The same condition was noted in other cases whenever a drain was removed. Several cases in the series above referred to showed a slight increase in the total number of leukocytes or in the polymorphonuclear leukocytes, during the course of convalescence, which could not be assigned to definite causes. These cases were few, and might have been caused by trivial changes in the patient's condition which were not noted or recognized.[1]

CASE II. (of same series) showed a relative increase in the polymorphonuclear leukocytes in the daily leukocytic count, which increase preceded all other signs or symptoms of a beginning suppuration of the abdominal wound. Frazier and Holloway report a similar finding in their cases.

One blood analysis in a given case may give data of the utmost value, or it may be of very little or of no importance in the case; if, however, two analyses are made within several hours, information may be gained which may precede all other signs or symptoms in the case. This is true in the class of cases referred to above —operative cases, and is therefore of great value to the surgeon.

The Duration of the Illness. Acute diseases with high fever do not produce marked changes in the erythrocytes; a slight increase from concentration of the blood may be found, which is very soon lost after the temperature returns to normal or when the fever becomes chronic in its course. The leukocytes in acute infections vary in number and in proportions, according to the nature and the severity of the infection and the resisting powers of the patient. In chronic infections the drain on the blood, as on other tissues of the organism, is more or less marked, depending in each case on the nature of that infection. The duration of the illness is of eminent importance and always to be considered in the class of cases which are infected by the usual pus-producing organisms. The acute stages of inflammation from the action of pus-producing organisms almost invariably show a leukocytosis. When the acute stages have passed, and the process becomes limited or localized; when pus is present and it becomes limited or walled-in (an abscess cannot be said to be walled-in until it has ceased to increase in size)—the leukocytic count may remain stationary; it usually decreases. The decrease in the count is generally gradual; this, however, depends upon the thoroughness with which the diseased focus is isolated from the healthy tissues. A normal leukocytic count, with a relative increase in the polymorphonuclear leukocytes or an absolutely normal count, may be seen in chronic inflammatory cases; however, counts ranging from 9000 to 12,000 leukocytes per cubic millimeter are usually to be encountered in this class of cases. The erythrocytes in chronic pus cases generally show more or less marked changes either in their number or in degenerations of these cells, depending upon the chronicity of the process and the drain on the general system. In fact, scarcely any disease has greater direct action on the blood as a whole than long-standing septic cases.

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[1] The cases from which these counts are taken were in the ward of Dr. Charles B. Penrose during the session of 1896–97. The counts were made twenty-four hours before the operation, within five hours after the operation, and then every twenty-four hours until the count returned to normal limits. No attempt was made at that time to complete the daily blood examination; consequently only the erythrocytic and leukocytic counts, estimation of the hemoglobin, cover-glass spreads, and notes of the cases were made. Later the differential counts were made and the daily notes compared with the findings in the blood. Since the publication of these cases similar work has been completed by Drs. Frazier and Holloway, with results similar to my own.

From these cases the value of comparing the blood-findings with what actually takes place in the patient is at once apparent.

Complications. During the course of a disease the occurrence of a secondary infection may completely alter the blood findings. How much these superimposed conditions counterbalance the blood changes in one class and exaggerate them in another is a very difficult matter to state. The blood changes in these conditions may be very different, even when the same type of a secondary infection is ingrafted upon dissimilar primary diseases. In tuberculosis the blood findings are only slightly changed from the normal as long as the process remains simple. As soon as a "mixed infection" complicates the original process, however, the blood findings immediately change, and the changes here follow more or less the type which is usually seen in septic conditions. A diverse reaction to a secondary septic infection has been noted in a marked degree in leukemia. Kormoczi reports a case of splenomyelogenous leukemia which, when first observed, showed 100,000 leukocytes and marked degenerations and reduction in the number of erythrocytes. During the observation of the case a septic condition of the nasal cavity developed. The blood examination during the septic infection showed a reduction of the leukocytes to 7300 cells per cubic millimeter (from 100,000) and an absolute disappearance of the degenerations in the erythrocytes, with the exception of a microcytosis.

In typhoid fever the value of the blood examination as an aid to the diagnosis, and during the course of the fever as a help in the diagnosis of complications, is of the utmost value. As an aid in the diagnosis of complications in this disease some knowledge of the previous condition of the blood should be known, for cases are reported with a leukocytosis running throughout the whole course of the fever and without discoverable cause. However, in typhoid fever the occurrence of a leukocytosis is generally assignable to some complication; therefore, before a leukocytosis which may occur during the course of a typhoid fever case can be of any value in the graver forms of complications in this disease all the causes for a leukocytosis in the case *must be considered.* In intestinal perforation a leukocytosis is the rule if the patient is reacting; no leukocytosis or a decrease in the number of these cells (in the great majority of cases) points to a severe asthenic condition of the patient, and therefore suggests a grave prognosis.

The hourly study of the leukocytes in typhoid fever, to endeavor to foretell a perforation, scarcely seems to be warranted by our present knowledge of the reactions of the leukocytes, during the course of this disease, to treatment and to other complications. It is true that in probably the majority of cases some change in the leukocytic count may precede all other signs or symptoms of a perforation. This change may not be in numbers only, but simply a change in the relative proportions of the different forms of the leukocytes, as in other cases cited above; but it must not be forgotten that the method of treating typhoid fever may play a very important part in increasing the number of leukocytes. The cold bath almost always produces a transient increase in the number of leukocytes. Other complications as hemorrhage and phlebitis usually produce a leukocytosis. I do not mean to say that a careful blood examination would not indicate in some way—probably very early—the occurrence of this condition, and therefore be of great value in directing treatment; but the necessity for absolute rest in these cases seems to me of more importance and of greater value in preventing such complications than are the early leukocytic counts, alone, in directing treatment—for the blood changes are only one of the signs which lead in each case to a diagnosis of this complication.

Finally, it must not be forgotten that physiologic influences produce definite changes in the blood, and should always be considered and excluded before the possible pathologic influences are given serious thought. Important among these are the time of day the examination is made ; the influence of muscular exercises ; the influence of profuse sweating; the effects of digestion, etc. The therapeutic action of drugs on the blood, as a whole, is more or less important, according to the class of drugs considered. In the individual case a drug may be a prime factor in causing the blood change, or it may lead to ambiguous results if not considered in the individual blood examination.

In conclusion: I have endeavored in discussing the role which the blood plays in the diagnosis of disease to present absolute facts, not hypotheses. Certain typical conditions almost invariably produce changes in the blood. These changes may be of a positive or of a negative value in the diagnosis of the disease. In some conditions the blood changes may absolutely clinch the evidence pointing to the diagnosis; in other cases, with our present knowledge, the blood offers absolutely nothing as an aid in the diagnosis. This, however, can be said of any branch of medical or surgical methods of examinations of which blood examinations are only a part. In any case, blood analyses, to be of any value, must be considered *only* in connection with the findings of other methods of examination, the history of the illness, and in the presence of complications. *February* 27, 1902.

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The Function of the Soluble Ferments of the Blood in Intracellular Digestion.

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The constituents of our food, viz., the proteids, fat, carbohydrates, and salts, are indifferent to oxygen outside of the animal organism, but readily combine with oxygen within the body. The sum total of the excreta incloses more oxygen than the sum total of the ingesta. As a certain amount of heat is generated and a certain amount of energy liberated during the passage of the food-material through the body, the whole process has been rather crudely compared to a combustion, life to a flame, the body to a machine, that burns the fuel that is fed to it. This conception is inaccurate, as it merely considers the most superficial manifestations of the life-process—the initial and the terminal stages of a most intricate process, the finer, intermediary mechanism of which we are just beginning to understand.

If we determine the quantity of oxygen inspired within a certain time unit and the quantity of oxygen excreted through the various emunctories of the body in the same time unit we will find that nearly 19 per cent. (that is, nearly one-fifth) more oxygen leaves the body than enters it in the inspired air. This can be explained only in one way, viz., some of the oxygen (one-fifth) contained in the excreta must be derived from another source than the air we breathe, and that other source can only be the food. We can go a step further and say that the oxygen present in the food must be torn out of its combination by a process that is akin to fermentation in its broader sense, and that consists in cleavage of proteid, fat, or carbohydrate molecules; this process, moreover, must occur without the intervention of free oxygen, must, in other words, be anaerobic and take place in a reducing medium.

As a matter of fact it can be shown that the assimilation and disassimilation of food occurs in two stages: (1) an anaerobic stage in a reducing medium without the intervention of oxygen and in the *interior* of the cells; (2) an aerobic stage in the presence of free oxygen (hemoglobin) at the *periphery* of the cell—*i. e.*, chiefly in the blood and lymph-stream. Both processes, it appears, are inaugurated by the intervention of soluble, chemical, unorganized ferments that the cells secrete—so-called "vital" processes are only indirectly concerned in these metabolic changes; for the present we are still forced to use the term merely to designate the power of cells in two directions, viz., (1) their power to build up active, functionating protoplasm from simpler, inert compounds; 2) their power to secrete enzymes with specific properties. Much that was heretofore considered "vital" has been robbed of this dignity by recent discoveries relating to the role of enzymes in "intracellular digestion."

The term intracellular digestion is employed in contradistinction to extracellular digestion to designate those processes of digestion or destructive metabolism that occur in all the tissues of the body other than the gastrointestinal tract—in reality it does not even exclude the processes going on in the mucosa and walls of the digestive canal, but merely those that occur in its lumen. As the material contained in the mouth, stomach, and intestine is not really within the body, intracellular digestion is essentially synonymous with general metabolism.

Leaving the fate of the inorganic constituents of the food out of our considerations we will briefly study how the molecules of proteid, fat, and carbohydrate material are rent asunder by the ferments, how the smaller torn-off molecules are recombined to form new compounds, how these are again disassimilated to simpler complexes, until finally some unfortunate atoms get out of their orbit, so to say, become chained to oxygen and stumble into compounds that have to be eliminated.

The fermentative changes occurring within the intestinal tract are essentially physical in character—*i. e.*, the proteids, fats, and amylaceous portions of the carbohydrates are hydrolyzed to compounds that can diffuse through animal membranes. The proteids are converted to albumoses and peptones (and in very small part to amido-products), the fats to fatty acids and glycerin, the starches to soluble sugars. That this hydrolysis is merely intended to enable the entrance of the original bodies into the organism proper is manifested by the fact that in their passage through the intestinal wall they are reconverted. Within and behind the intestinal wall—*i. e.*, in the blood of the mesenteric veins and the lacteals, we never consequently encounter peptone or albumose, but only serum-albumin; the same in all probability applies to the fats; glycerin and fatty acids being recombined to neutral fat in their passage through the intestinal wall. Whether or not the sugars enter the blood and lymph directly is not positively determined; a great portion of these sugars certainly reaches the liver as glycogen and is deposited there as such.

This process of reconversion has recently been shown to be due to enzyme action. It appears that the same ferments that can split fat, *e. g.*, into glycerin and fatty acids, possess the power of recombining glycerin and fatty acids to neutral fat. This process also occurs *in vitro* by the action of lipase, the ordinary fat-splitting ferment of the pancreas (steapsin). The discoverers of this "reversion" process determined, moreover, that lipase is concerned in bringing about a condition of chemical equilibrium between the fat molecule (and water) and the products of its hydrolysis; in other words, that it forms a certain proportion of fatty acids and glycerin if neutral fat is present in excess, but that it is also inversely capable of forming a certain proportion of neutral fat from glycerin and fatty acids, provided the latter bodies are present in excess in the solution.

The one objection to this theory is the fact that we cannot identify ferments in any other way than by their manifestations; we have, moreover, no way of isolating them from the organ-extracts in which they are dissolved. It is not impossible, therefore, that pancreatic extract, or even so-called "pure" lipase, contains two ferments, the one that splits fats to glycerin and fatty acids, the other that recombines the two to fat. This objection is strengthened by the observation that a ferment other than pepsin or trypsin, namely rennet, seems capable of reconverting albumoses and peptones to coagulable albumin. If egg albumen or fibrin are digested with artificial gastric juice (pepsin, HCl) and the albumoses and peptones that are formed removed by dialysis (a process analogous to the removal of these products from the intestine by osmosis through the intestinal wall), and if to the dilute clear solution of albumose-peptone some rennet is added, a flocculent coagulate of albumin will reappear. As rennet is a normal constituent of the gastrointestinal mucosa, it seems probable that this ferment is concerned in regeneration of serum-albumin from albumose-peptone.

The question arises, where do these processes occur? in the mucosa, the muscularis, the serosa, the lymph, or blood-stream? Presumptive evidence is overwhelmingly in favor of the supposition that the leukocytes in the blood and lymph capillaries of the intestinal wall are in some way concerned in this process (digestion-leukocytosis); we will revert to the role of these cells as ferment-carriers later on, and show that disintegration of leukocytes, as a rule, precedes the inauguration of many fermentation processes, a disintegration that probably precedes or is accompanied by a liberation of enzymes. We will also attempt to ascertain the source and origin of the ferments that the leukocytes harbor in their interior, and that they carry to any portion of the body where they are needed to establish chemical equilibrium. All the ferments are so toxic when circulating freely, and are still so universally present that we can only assume that mobile cells like the leukocytes bear them in a harmless form through the blood and lymph-stream to their ultimate destination.

Of the food albumin that circulates in the blood and lymph-stream as serum-albumin, only a very small proportion is built up directly into living protoplasm. The cell-protoplasm seems endowed with considerable longevity, so to speak, for only 16 to 20 grams of cell-protoplasm "die" in twenty-four hours—a remarkably small proportion in an organism weighing from 70,000 to 75,000 grams. From these figures we know that only 16 to 20 grams of the circulating serum-albumin are directly incorporated into the cell body, are, so to say, endowed with life, and become living protoplasm to take the place of that quantity of protoplasm that dies and is cast off into the blood-stream.

The great bulk of the albumin, fat, and carbohydrate is simply food for the cells and the source of the energy they require. With the aid of the enzymes they secrete they split the large molecules. This process occurs in two stages: the first process is a reduction, and like every reduction requires heat—the result is the formation of numerous compounds that possess greater affinity for oxygen than the original bodies; the second process is an oxidation in which the chemical affinities are satisfied and heat is developed—the result is the formation of highly oxidized compounds that are excreted. The whole process then is a vicious circle—the heat that is converted into chemical affinity is derived from the oxidative processes that satisfy the chemical affinity; once inaugurated, the process goes on indefinitely, provided sufficient potential energy is introduced with the food that can be converted into kinetic energy.

This chemism is altogether analogous to similar processes occurring in the inorganic world. In order to reduce oxid of potassium—*e. g.*, with carbon—heat is required: the result is metallic potassium that possesses great affinity for oxygen. If potassium is oxidized again the same amount of energy is liberated that was originally required for the reduction. We need not postulate any specific "vital" force; the universal laws of the conservation of matter and of energy operate in the same way in the organic as in the inorganic world. Living plants and animals merely possess specific powers of combining and converting matter and of transmitting energy into specific forms of motion that we call vital.

It would lead us too far were we to follow the step-wise degradation of the albumin, fat, and carbohydrate molecules in detail. It may suffice to study the principal products of the first anaerobic reducing stage and of the second aerobic oxidizing stage, and to elucidate, as far as we are able, the ferment mechanism of these conversions.

A clear insight into these processes can be gained by drawing analogies with similar biochemic reactions that are carried on by unicellular microorganisms. The animal body, after all, is merely a conglomerate of numerous unicellular microorganisms, in which each cell is a special microlaboratory and leads an independent existence, while at the same time contributing its share to the maintenance of the whole. Unicellular organisms are so small, as compared to complex multicellular organisms, and the metabolic changes they bring about in the media they grow in are so colossal in comparison to their bulk, that we are apt to overlook the fact that these metabolic processes are merely incidental and certainly subservient to the biologic needs of the cells. The character of the protoplasm of bacteria and of our body cells, moreover, is different only in distribution and not in character.

As a prototype of anaerobic life, as an illustration of the first reducing stage of metabolism, the life-processes of Tyrothrix urocephalum, a bacterium that has its natural habitat in putrefying milk, may be studied. This germ, when grown on milk, attacks the proteids of the milk alone and leaves the fats and carbohydrates intact. If oxygen is excluded it splits the proteid molecule, combines some of the carbon with some of the oxygen, and generates CO_2; combines hydrogen with oxygen and forms water; secretes a proteolytic enzyme that converts other portions of the proteid molecule into peptones and then into urea, fat, ammonia compounds, tyrosin, a variety of ptomains, and certain intermediary acids. This germ requires some oxygen, but it can derive it from the oxygen atoms contained in the proteid molecule; the oxygen is needed, not for the metabolic processes that are carried on by the enzyme the bacterium secretes, but for the maintenance of its scanty life-processes.

Altogether analogous processes are carried on by the cells of the animal body. If a piece of muscle be kept in a vacuum at a body temperature CO_2 will be developed and water will be formed. There is evidence to show that the fats and carbohydrates are not disassimilated in this first stage, but that the proteid molecule alone is attacked, and that it is converted into urea, glycogen, and fat, ammonia products, leukomains, and a large variety of intermediary bodies. These processes have been studied particularly in the liver, but it can readily be shown that similar processes occur in other organs of the body, and it is probable that this form of activity is a universal property of all our cells. During life all these intermediary products are immediately oxidized, so that it is a very difficult task to detect them. In certain diseases and intoxications, however, in which the aeration of the blood is interfered with, in dyspneic states, in the agonal stage, or immediately after death, when the individual cells still live, although the blood no longer circulates, these products accumulate very rapidly in the tissues and can be detected there. The reducing properties, finally, of nearly all the organs of the body have been repeatedly demonstrated by coloring methods

(Ehrlich), and feeding and injection experiments with iodates, indigo, certain pigments, etc.

The chief products of this first stage are carbon dioxid (CO_2), water, urea, creatin, etc., on the one hand, and a large number of intermediary products on the other. The former must be considered "rests," waste products, so to say, that have to be eliminated. Many of the intermediary products travel to the liver and are there forced into new combinations; some form urea, some uric acid, etc., but the majority of the fats, carbohydrates, hydrocarbons, amido acids, together with the original fats and carbohydrates of the food, undergo oxidation in the blood-stream.

Whereas, we have so far been unable to demonstrate experimentally that the cells of our body, like certain bacteria, of which Tyrothrix urocephalum is the prototype, secrete enzymes that bring about the processes of proteolytic anaerobic fermentation that we have discussed, we are able to show experimentally that the second (oxidative) stage of disassimilation of fats, carbohydrates, etc., is due to the action of numerous soluble ferments that are present in the blood and lymph.

If blood or lymph is allowed to flow directly into a sterile vessel, and the vessel allowed to stand for a number of hours at body temperature, a progressive loss of the blood-sugar will be observed. Occasionally a slight *increase* in the titer for dextrose will be noticed during the first half-hour, followed, however, by a rapid decrease during the hours following. This preliminary increase only occurs when the blood contains some glycogen, and is explained by a preliminary conversion of glycogen to dextrose. Here, then, we see the action of two ferments, one that can convert glycogen to sugar (an amylolytic ferment) and one that can destroy sugar. We can go still further. If we analyze the sugar that is formed from glycogen in the blood we will find that it consists in part of maltose (a double sugar), in part of dextrose (a simple sugar). By allowing blood to flow into alcohol, and leaving the coagulate that forms in contact with alcohol, we destroy the power of the blood to form dextrose, and only maltose is formed from glycogen. In other words, the blood contains both a *maltase* and *glycase—i. e.*, a maltose- and a dextrose- (glycose) forming ferment, the latter being destroyed by contact with alcohol (Bial). If chylus fat is mixed with blood or lymph, and if the mixture is allowed to stand at body temperature, some of the fat will be destroyed and be converted into hitherto unidentified bodies (possibly fatty acids and glycerin) that, in contradistinction to fat, are in large part insoluble in ether and are dialysable.

Another ferment called oxidase is present in the blood and lymph that possesses the power of oxidizing a number of organic substances, and, besides, pepsin and trypsin in appreciable quantities, not to speak of the so-called fibrin ferment.

The questions arise, In what constituent of the blood do we find these ferments, in the serum, the red or the white blood-corpuscles; where do they come from, what is their ultimate fate?

If the blood is centrifuged and serum and corpuscles examined separately, it will be found that the serum possesses neither diastolic, glycolytic, nor lipolytic properties; an extract made from the corpuscles, on the other hand, does possess these properties to a marked degree. If a piece of one of the veins of a large animal is ligated in two places and incised, then suspended in the ice-chest for twenty-four hours, coagulation of the blood does not occur, and, under favorable conditions, red corpuscles, white corpuscles, and serum can be aspirated separately. It will be found that the ferment power is inherent in the white and not the red cells. When we consider, in addition, that the lymph possesses still greater glycolytic and lipolytic powers than the blood, when we remember the phagocytic action of the leucocytes toward all poisons (and the ferments are very toxic), we will agree that these ferments are carried by the leukocytes. As a matter of fact, leukocytes possess distinct digestive powers toward bacteria. Finally, if chemotactic bodies are added to the blood that promote rapid disintegration of leukocytes, the ferment powers of the blood are more rapidly developed, all of which seems to justify the conclusion that the ferments are carried by the leukocytes and that disintegration of leukocytes must precede the liberation of the ferments.

Some investigators claim to have found the ferments in the serum, and, as a matter of fact, they are frequently there, but only after the leukocytes have begun to degenerate, an accident that can hardly be avoided when the blood is subjected to such manipulation as defibrination, centrifugation, etc.

The origin of these blood ferments is obscure; there are three possibilities: they can either be formed in the leukocytes themselves, they can be formed in all or many of the tissues and organs of the body—*i. e.*, by protoplasm in general—or they can be derived from internal secretions of the digestive glands. It is altogether impossible at present to decide this question. In view, however, of the tendency to specialization that becomes operative in any large congregation of individual cells, the latter view is the most plausible—the digestive glands would then furnish enzymes both for extra- and intracellular digestion.

Whether the blood ferments after they perform their functions are destroyed, eliminated, re-inclosed in leukocytes, or arrested in the digestive glands to be re-excreted, or, finally, are held by such disintoxicating organs as the suprarenals, the thyroid, and the liver, it is impossible to say. As the urine nearly always contains some of the ferments, as they are nearly always present in the liver, and as they certainly must suffer the ultimate fate of all the other constituents of the body, it is probable that all these processes can and do occur.

It has been objected that the ferments are present in such minute quantities in the blood that they can impossibly be credited with an important role in intracellular digestion; but this objection is invalid. In the first place, they are present in minimal quantities in the extracts we prepare, because they are not intended to be present in large quantities at any time, nor to be copiously *excreted* like the digestive ferments; they are, as we have said, toxic in large quantities. When we prepare our extracts we destroy the cells and *force* the ferments into solution; besides, we work with small quantities of blood, and consequently very small numbers of leukocytes. In studying the action of such an extract, moreover, we see only a small portion of the power that would have been expended had the cells remained intact, had the blood remained alive. I can best illustrate this by comparing the action of the ferment extracted out of a kilo of yeast cells and the action of a kilo of living yeast cells. The ferment solution will develop less power by far than the living cells, as in the latter new ferment is continually being formed; in other words, the action of the ferment accumulating during an hour is only a small proportion of the hourly action of the cells. The ferment solutions from the blood only contain the remnant that is not utilized during life.

Furthermore, nearly all ferment extracts are made after defibrination or alcohol coagulation, and it is a well-known fact that fibrin and coagulates retain ferments with a tenacity that makes it almost impossible to separate the two; in this way, too, a large proportion is lost.

From very recent investigations it appears that the ferments are chemically (if they are chemical entities at all!) nucleoproteids—*i. e.*, derivatives of the cell nuclei. They are in general so akin to protoplasm both in their chemical reactions and their behavior to various physical and chemical agencies that they must be considered closely related to living protoplasm. As a matter of fact, all protoplasm has some ferment power; ferments seem to be fragments of protoplasm and living protoplasm can do all that ferments can do and more besides in other directions, viz.: it has the power of regeneration (see above) and of "assimilation."

Some investigations that I am at present engaged in seem to point to a still closer connection between ferments and living protoplasm even in its most "vital" properties. If 0.01 grain of pepsin is dissolved in 95 c.c. of a 2.75 per cent. solution of HCl and 5 grams of fibrin or egg albumen added the fibrin will be digested within twenty-four hours and the fluid will become clear; of this fluid 10 c.c. are mixed with 85 c.c. of HCl solution and 5 grams of fibrin added again; this, too, will be digested. This process of dilution can be repeated many times and the digestion of fibrin will proceed almost as rapidly as in the beginning; not until the ninth or tenth dilution will an appreciable retardation become noticeable. If we calculate the dilution we will find that one part of the pepsin seems capable of digesting many million parts of fibrin. If the same dilutions of pepsin solution are made without adding fibrin and permitting digestion for twenty-four hours, it will be found that no solution of the fibrin occurs after the dilution is greater than 1 to about 30 to 50,000. (This applies to the particular pepsin I am using.) The whole process resembles a regeneration of pepsin by contact with fibrin; in other words, a growth in a suitable medium. In the absence of pabulum no growth occurs.

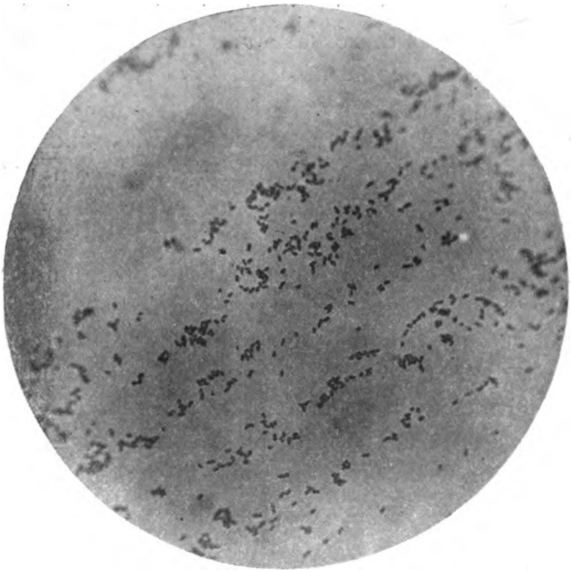
If these findings can be verified and amplified and extended to other ferments, they promise to carry us several steps forward into the borderland that lies between dead and living protoplasm.

February 27, 1902.

A Preliminary Report on Microbacilli in the Sebaceous Glands of the Nose, with Demonstration of the Alleged Germ of Seborrhea and Baldness.

JAY F. SCHAMBERG, M.D.

About a year ago, while examining the sebum from the sebaceous follicles of the nose, I noticed the presence of a minute bacillus which was apparently identical with an organism described by Unna, Engman and Hodara in 1894, and constantly found by them in blackheads. On investigating the subject I learned that Sabouraud had previously noted the presence of this bacillus in the sebaceous glands of this region, and had remarked upon the identity of this organism with that of Unna. Unna and his confreres regarded this bacillus as the cause of comedones and of acne.



Microbacilli in sebaceous material from nasal follicles (Microbacillus of Seborrhea. Sabouraud). Zeiss 1/12 oil immers. Zeiss proj., ocular 4.

In order to determine its frequency I examined fifty subjects, some perfectly healthy individuals and others suffering from various cutaneous diseases, presenting themselves at the Polyclinic Hospital. A little sebum was squeezed out from the nasal follicles, spread between two cover-glasses, and stained with Loeffler's methylene blue and gentian violet. The condition of the skin of the nose, whether oily or dry, was noted in each instance. The results are herewith subjoined: Bacilli were present in forty-five cases and absent in five; they were present, therefore, in 90 per cent of the patients examined:

Positive cases, skin oily	27	
" " " dry	16	
" " not determined	2	—45
Negative cases, skin dry	3	
" " " oily	2	—5

In the negative cases there was some difficulty in getting a sufficient amount of sebaceous material. No re-examinations were made.

The bacilli were present in masses of thousands, and represented practically pure cultures. They varied from 1¼ to 1½ μ in length and ⅓ to ½ μ in width; they were easily stained with anilin dyes, but were decolorized by acids.

Stained with Loeffler's methylene blue or thionin they were very minute. They were about one-third larger when colored with gentian violet, owing to the staining of the surrounding capsule. They were not decolorized by Gram's method.

Efforts to artificially cultivate this bacillus failed. After trying all the ordinary media I employed sterilized butter and a combination containing chlorid of sodium, phosphate of sodium, lanolin, etc., to approximate the constitution of human sebum, but without success.

According to Sabouraud the microbacillus of seborrhea, as he terms this organism, presents young and adult forms. The young forms are punctiform. Under high power they are seen to have an ovoid shape. A careless examination might lead to their being regarded as cocci. Their long diameter is less than a thousandth of a millimeter. The adult forms are longer, often sigmoid, and present about the appearance and dimensions of the tubercle bacillus. Sabouraud has succeeded in growing this bacillus upon a special medium after fifteen months of experimentation. The following is the formula of the culture medium employed:

Agar-agar	1.5 grams.
Granulated peptone (Chassaing, Paris)	20 "
Neutral glycerin	20 "
Distilled water	1 liter.
Acetic acid (crystal)	5 drops.

The tubes often show at the end of two days round, gray, creamy, flat colonies, which result from the growth of a coccus frequently found upon seborrheic skins. The microbacillus shows its first development only at the end of four days. The adult colonies at the end of twenty days appear as a brownish or rose-brick conical or button-like elevations raised 1 to 3 mm. above the level of the culture medium. Growth continues for a period of five weeks.

The organism may also be grown by inoculating the center of an egg. In two months the yolk of the egg is converted into a solid reddish-brown block of tissue which gives off a peculiar aromatic odor.

Animal inoculations on the surface of the skin of the horse, sheep, dog, guinea-pig, and rabbit have remained negative. Liquid cultures injected subcutaneously have given rise to loss of hair, at times diffuse, and at other times in circumscribed areas. It is admitted, however, that the hair-fall may have resulted from inflammatory reaction produced by the injected fluid. Large injections do not seem to have destroyed the life of the animals, although emaciation was produced in some for several weeks.

Seborrhea. Sabouraud considers the presence of sebaceous filaments in the skin as the essence of seborrhea. These vermicelliform masses of sebum are the forerunners of blackheads. In both of these conditions the sebum contains millions of microbacilli. Sabouraud remarks that "this is, at the same time, the purest and the most abundant cutaneous infection known." For him this bacillus is likewise an accessory, and even at times the exciting cause of acne. "There is no acne without pre-existing seborrhea." The formation of the acne papule and pustule is due ordinarily to secondary infection with staphylococci. Suppuration may, however, result at times without such secondary infection. "One is thus persuaded to ask," says Sabouraud, "whether in some cases acne suppuration is not purely microbacillary."

Baldness. According to Sabouraud, baldness is also due to this microbacillus, although he recognizes predisposing causes. He says: " I have never seen a baldness which was not microbic and which did not present the same microbe always present in the follicle from which the hair falls." " True baldness is seborrheic. Finding the microbe of seborrhea on the scalp of all bald persons proves bacteriologically the identity of oily seborrhea in all of the regions that it may occupy."

ALOPECIA AREATA. Several years ago Sabouraud described a microbacillus in the dilated summits of the hair follicles in all cases of alopecia areata. He regarded this organism as, in all probability, the cause of the disease. This bacillus cannot be distinguished, morphologically or tinctorially, from the organism described by Unna, and found in seborrhea, blackheads, and ordinary baldness.

I am of the opinion that this small bacillus may be found in the sebaceous follicles of the nose, and perhaps of other regions, in 90 per cent. or more of adults.

If microbacilli are present in millions in the sebaceous gland of the nose in nearly all adults, it is not surprising that they should constantly be found in comedones and frequently in the hair follicles of the scalp. Sabouraud first found them in alopecia areata, and more recently in ordinary baldness. It will be interesting to determine whether they cannot be found in other conditions.

Are all individuals in whom microbacilli are found protected against acne, baldness, and alopecia areata by reason of the fact that they present an unfavorable soil for the growth and development of this bacillus? If this were true it would indicate that only a very small percentage of the carriers or hosts of this organism were susceptible to its ravages. Moreover, the vast majority of people, in addition to this minute bacillus, have staphylococci present upon the skin. They have, therefore, both of the germs which determine an acne. If they are protected by the absence of favorable soil, then the general predisposing causes of acne are of preponderating importance and the presence of the exciting organisms of secondary significance.

In the sebaceous follicles of my own nose and in those of the various members of my family I have repeatedly found myriads of microbacilli. I believe most physicians will be able to verify this observation in their own households.

Sabouraud explains the origin of microbacillary infection in the following manner: "By chance contact—such, for instance, as might occur in kissing—the bacillus passes from one individual to another. It may or may not find a favorable soil. If it does find it it multiplies in the sweat and the sebum exuded upon the surface of the skin. It multiplies until it reaches the orifice of a follicle in which its generations can live."

"The microbacillary infection, once established in the follicle, is invariably accompanied by three symptoms: the seborrheic flux, the falling of the hair in the infected follicle, and the hypersecretion of the sweat glands in its neighborhood." One must admire the industry and the close powers of observation which have enabled Sabouraud to elaborate the fascinating theory which he presents in his recent most interesting work, *Les Maladies Seborrheiques*. It appears to me, however, that the evidence presented as to the parasitic nature of seborrhea, acne, and baldness is by no means conclusive. It has not been definitely proven that the microbacillus described by Unna and Sabouraud is not a more or less normal resident of large sebaceous glands.

March 27, 1902.

A Renal Calculus Composed of Calcium Oxalate, Calcium Carbonate, and Magnesium Phosphate.

DAVID RIESMAN, M.D.

The small stone I here exhibit was passed *per urethram* by a man, forty-six years of age, who had been suffering with symptoms of stone in the right kidney for six months. His first attack of pain came on last June, after considerable exposure during a fishing expedition in the mountains. He had a number of attacks of pain, not distinctly colicky, but associated with vomiting. During the intervals he felt well, except for a sense of soreness in the right loin. He had not had hematuria up to the time when I first saw him, which was about the end of October. During the attacks the urine was scanty, but became copious immediately afterward. The only other symptom that he had noticed since the first attack of colic was a desire for frequent micturition after coitus. The urine at first presented nothing abnormal except a slight trace of albumin on one occasion.

In November, without having had an attack of colic, he passed some large reddish shreds, which, on naked-eye examination, looked like coagulated blood. The passage of shreds continued for three days. The urine at this time was of a turbid amber color and contained half a grain of albumin to the liter by the Esbach albuminometer. Microscopically, the shreds consisted of red and white blood-corpuscles and large irregular cells, with a large nucleus, that appeared to be epithelial. The urine was always acid, but not strongly so. Three weeks later he had a mild attack of colic, and twenty-two hours later, without any especially severe pain, passed this stone. It is of a light, grayish-brown color, has a coarsely granular surface, and is about as large as a dried pea. The interior is grayish-white. Chemical examination shows it to be composed of calcium oxalate, calcium carbonate, and magnesium phosphate.

Since the passage of the stone the man has had no pain in the back, and is now perfectly well. It is surprising how much trouble a small calculus may cause.

The subject of renal stones has not received as much attention from scientific investigators as that of gallstones, and our knowledge is largely confined to chemical composition, being quite incomplete as to sources and modes of formation.

Ebstein and Nicolaier,[1] in some important experimental studies, as well as Posner,[2] showed that renal calculi have an organic framework in which the lithogenic substance is deposited. The framework is of an albuminous nature, has the outlines of the stone itself, and can be demonstrated by staining after solution of the calculous matter.

It is customary to divide stones into primary and secondary varieties, the former comprising, according to Morris,[3] calculi formed in healthy kidneys, independently of any preceding change in the organs or of any septic condition in the urinary passages; the latter, those occurring in kidneys previously diseased, and resulting secondarily from septic processes in the pelvis and calyces.

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[1] Ebstein and Nicolaier. Congress f. innere Medicin, viii.

[2] Posner. Quoted by Rosenstein, Pathologie u. Therapie der Nervenkrank., 1894, 594.

[3] Morris. Surgical Diseases of the Kidney and Ureter, 1901, vol. ii. 43.

The etiology of primary calculi is virtually unknown. Bacteria have of late, as in the case of biliary calculi, been held responsible for their formation; but while some observers found micro-organisms others did not, particularly not in one of the most frequent primary calculi, that of uric acid. Foulerton[1] found the Bacillus coli communis in the interior of four out of seven stones examined, the stones having been obtained either during life by operation or after death at autopsy. He does not, however, attribute any etiologic importance to the colon bacillus in connection with renal stones, but is of the opinion that an infection of the kidney by the bacillus sometimes occurs early in the history of a calculus, and that the organism thus becomes enclosed within the growing stone.

There is a difference of opinion regarding the frequency of the various types of stone, but statistics seem to show that the calcium oxalate calculus is the most frequent. Pure calculi are very rare, the majority being composed of several constituents, the principal one of which governs the designation of the stone. Next in frequency to the oxalate stone is the uric acid calculus, which, according to some authorities, is, indeed, the most common variety. Uric acid stones are more often bilateral than those of oxalate of lime; hence the fact that my patient passed one of the latter type encourages the belief that the other kidney is unaffected.

While in bilateral lithiasis the stones are usually of the same nature, they at times differ, and Israel,[2] in two cases, found a calcium oxalate stone associated, in the one case, with a calcium phosphate calculus, and, in the other, with one of calcium carbonate.

March 13, 1902.

Large Ovarian Cyst.

M. H. FUSSELL, M.D.,
AND
THOMPSON SCHELL, M.D.

The patient from whom the tumor was removed was seen with Dr. John Woodruff, of Roxborough, to whose kindness we owe the privilege of showing the specimen.

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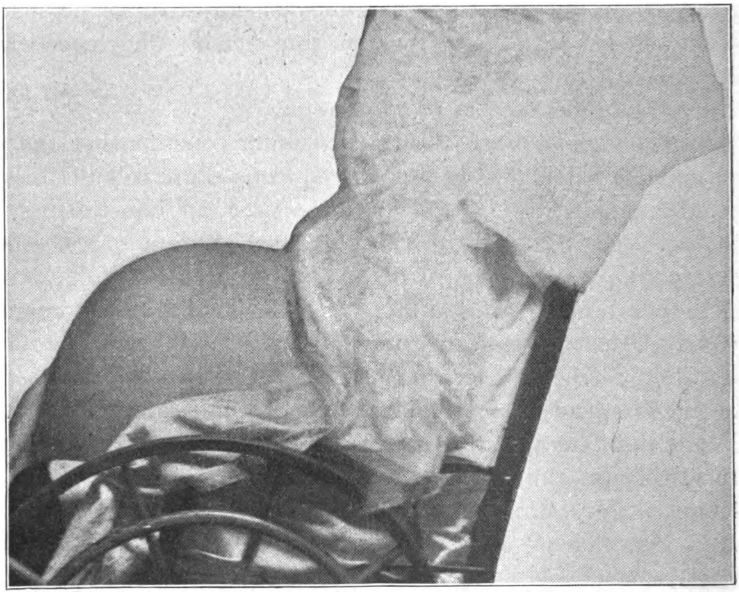
[1] Foulerton. Quoted by Morris, Surgical Diseases of Kidney and Ureter, 1901, vol. ii. 47.

[2] Israel. Chirurgische Klinik der Nierenkrankheiten, 1901, 278.

Mrs. M., aged forty-seven years; has one child aged twenty-eight years. She was always in good health until seven years ago, when she developed an umbilical hernia. The appearance of the hernia was followed by a gradual enlargement of the abdomen. The enlargement increased gradually until one year ago, when it reached about the size it is at present. The patient has been gradually becoming more helpless. She has not been out of the house for two years. She still goes up and down stairs, but with much difficulty. She cannot lie flat in bed, but has to sleep sitting up. Three days before the reporters saw her she consulted Dr. Woodruff for severe pain in the abdomen, with persistent vomiting. Her pulse was feeble, rapid, and irregular. Her bowels were obstinately constipated. There was evidently acute intestinal obstruction.

FIG. 1.



Showing size of abdomen. Patient in chair.

When seen she presented much the appearance shown in the photograph. The picture does not show the deformity in its extreme contrast to the chest and limbs, on account of the fact that the photograph was taken while the patient was extremely ill and was forced to sit up. It will be noticed that the anterior wall of the abdomen reaches to the knees.

On examination the following notes were made:

The tumor extends in a straight line from the anterior superior spine of the ilium 37 cm. The girth of the abdomen is 170 cm., or 6 feet 3 inches. There is marked edema of the abdominal walls; tremendous distention of the superficial veins in the abdomen. Some of these veins measured 1 cm. in diameter. Great edema of the lower limbs.

Heart. The cardiac impulse is diffuse; the lower limit of the impulse is at the fourth rib; the apex beat is in the third interspace, just inside the midclavicular line. The heart dulness is to the *right* edge of the sternum, the *second* rib, and midclavicular line. Heart sounds rapid, regular, free from murmur except at the extreme left border, where a soft systolic whiff is heard. First sound fairly strong; second sound much accentuated.

Lungs. There is a resonant note, with good breath sounds in the upper portion of both lungs. The bases of both are dull; here there are poor breath sounds and a few subcrepitant rales.

There is slight fever. Vomiting still continued.

In view of the fact of the danger of death in a few hours if no interference were practised, the patient was removed to a private room in St. Timothy's Hospital. The same evening sudden increase of the symptoms occurred, pulse became feeble, vomiting persistent and became stercoraceous, pain extreme.

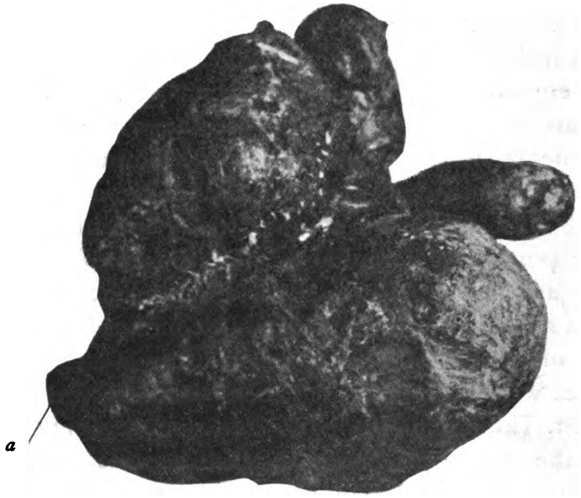
The cyst was immediately tapped, and eighty-six pints or about ten gallons of fluid withdrawn in the course of an hour.

There was no shock. In opening the belly wall for tapping it was noticed that part of the sac was gangrenous.

The next morning an operation was undertaken with the hope of removing the gangrenous sac. There was so much inflammatory condition and the adhesions were so great that the operation was not continued to the end, though this large portion of the sac was removed. It was gangrenous on the portion presenting at the umbilicus. This mass was the right ovary. The tumor consists of four lobes, two composing the bulk of the tumor. From the larger end of these lobules spring two daughter cysts, one of which is sausage-shaped, and measures eight inches in length and two and one-half inches in diameter. The whole mass measures forty-three inches in circumference in one direction and forty-two inches in the other. There are many daughter cysts in the interior. At the operation a large cyst was found to occupy the seat of the left ovary. The patient lived several hours, but died suddenly in a convulsion.

The fluid removed at the tapping was thickish, of reddish chocolate color, with the odor of fresh blood. Microscopic examination of the fluid shows very numerous, slightly crenated red blood-corpuscles. There is a large number of masses which have the appearance of large pollen grains.

FIG 2.



a. Portion presenting at umbilicus.

The weight of the sac removed was seven and three-quarters pounds. This added to the weight of the liquid made the weight of the material removed one hundred pounds. Such immense tumors are now fortunately rare in this country. Kelly, in his work on *Operative Gynecology*, figures such a case as this, and says: "Tumors weighing over fifty pounds are rare, but well authenticated cases are recorded in which the weight has exceeded one hundred and fifty pounds." *April* 10, 1902.

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The Intercommunicability of Human and Bovine Tuberculosis.

MAZŸCK P. RAVENEL, M.D.

(*From the Laboratory of the State Live-stock Sanitary Board of Pennsylvania*).

I find it difficult to express adequately my deep sense of the honor which has been paid me by the invitation of your committee to give the address of the evening on this occasion. The Pathological Society of Philadelphia has from its foundation had a most honorable position among the scientific bodies of the world, and has always stood for what is best and most advanced in the branch of medical knowledge to which it is particularly devoted. I have always felt it a high privilege to be able to inscribe myself a member, and to have the seal of the Society put to such contributions as I have been able to make. More than this I never thought of aspiring to, hence the invitation to give this address was as unexpected as it was grateful to me.

The hesitation which I naturally felt over accepting such a responsible office was relieved, to a considerable extent, by the suggestion of your committee that I should speak on some phase of the tuberculosis problem, which has been an object of special study at the Laboratory of the State Live-stock Sanitary Board of Pennsylvania, and in which I have had the constant advice and assistance of Dr. Leonard Pearson, State Veterinarian of Pennsylvania, and Dr. S. H. Gilliland, First Assistant. The work I am about to report from our laboratory is the result of our joint efforts, and I take pleasure in acknowledging my personal indebtedness to these coworkers.

The past decade has seen the awakening of a wide-spread interest in the study of tuberculosis, the spirit of Oriental fatalism which has for so long led us to view with equanimity the awful loss of life annually inflicted by this great white plague having given way to an active campaign against its ravages, a campaign so far largely one of education, in which we strive to spread far and wide the fundamental facts that tuberculosis is a communicable disease, and, from that fact, preventable. If preventable, why not prevented? With these precepts firmly implanted in the minds of the medical profession, as well as of the general public, we have reason to hope that each year will see a more careful study of the methods by which tuberculosis is spread and the means to be adopted for its prevention. On every hand societies for the prevention of tuberculosis are being formed whose object is to teach the truth concerning the disease and to dispel those false notions, chief among which may be mentioned belief in the hereditary character of tuberculosis, which in the past have led us to regard the tribute of human life as inevitable.

The intelligent prophylaxis against any disease demands a thorough understanding of the methods by which it is spread. The whole world is in accord in assigning the chief rôle in the propagation of tuberculosis to the inhalation of particles of sputum thrown off by phthisical persons, the majority of the profession agreeing with Cornet in the belief that sputum is most dangerous when dried and pulverized, while others follow Flügge in regarding the moist floating particles thrown out during coughing, sneezing, etc., as most to be feared. The danger to mankind from tuberculosis of cattle has been discussed at a length and with a fervor not surpassed in the history of modern medicine. The immense practical importance of the subject to the medical profession, to those charged with making and enforcing laws for the preservation of the health of the community, no less than to every man, woman, and child, justifies our deepest interest, and most earnest studies.

The relation that exists between human and bovine tuberculosis and the part played by cattle in spreading the disease among mankind is now the great question, to which attention has been drawn with renewed activity by the attitude of Professor Koch, announced in his paper before the British Congress on Tuberculosis in July, 1901. This paper was the more striking in that it contained statements diametrically opposed to the former teaching of Koch that "Bovine tuberculosis is identical with human tuberculosis, and is thus a disease transmissible to man."[1] This belief was the outcome of the experiments made by Koch at the time of his discovery of the tubercle bacillus, and has been generally accepted by the medical and veterinary professions up to the present time. So much has been written of late on the subject that I will pass over minor differences of opinion, and at once take up the consideration of the two main propositions which were formulated by Koch, and which include all points of controversy in the discussion of the relation between human and bovine tuberculosis.

1. "Human tuberculosis differs from bovine and cannot be transmitted to cattle."

2. "Though the important question whether man is susceptible to bovine tuberculosis at all is not yet absolutely decided, and will not admit of absolute decision to-day or to-morrow, one is, nevertheless, already at liberty to say that if such a susceptibility really exists the infection of human beings is but a very rare occurrence. I should estimate the extent of infection by the milk and flesh of tuberculous cattle, and the butter made of this milk is hardly greater than that of hereditary transmission, and, therefore, do not deem it advisable to take any measures against it."

I. The first of these propositions is susceptible of direct experimental investigation, and can, therefore, be answered positively without going into the domain of theory. Prof. Koch based this statement on the result of an insufficient number of experiments done by Prof. Schütz and himself. A number of young cattle proved to be free from tuberculosis by the tuberculin test were infected in various ways with the bacilli of human origin or with tubercular sputum. "In some cases the tubercle bacilli or the sputum were injected under the skin, in others into the peritoneal cavity, in others into the jugular vein. Six animals were fed with tubercular sputum almost daily for seven or eight months; four repeatedly inhaled great quantities of bacilli, which were distributed in water and scattered with it in the form of spray. None of these cattle (there were nineteen of them) showed any symptoms of disease, and they gained considerably in weight." After six to eight months they were killed, and no trace of disease was found in the internal organs. Where the injections were made small foci of suppuration had formed, in which there were found a few bacilli.

Inoculations of a similar nature with bacilli from the lungs of an animal with bovine tuberculosis resulted always in rapid illness, ending often in death, while some were killed in a miserably sick condition after three months. In all cases there was extensive tuberculosis, involving the internal organs, especially the lungs and spleen.

A similar difference in pathogenic power was found in feeding experiments on pigs, where one lot of six received human tubercular sputum, and a second lot of six were given pure cultures of the bovine tubercle bacillus; and also in experiments on asses, sheep, and goats, where the inoculations were made with pure cultures of human and bovine bacilli into the circulation.

Results similar to these in the main have been obtained by Smith,[2] Frothingham, Dinwiddie,[3] and at the laboratory of the State Live-stock Sanitary Board of Pennsylvania,[4] and we may admit that, as a rule, cattle show a high degree of resistance to the human tubercle bacillus, and that for all experimental animals the bovine bacillus has a pathogenic power equal to the human bacillus, while for the great majority it is vastly more pathogenic; but this does not by any means show that man is not susceptible to infection by the bovine organism, and we have abundant proof that it is quite possible to infect cattle with the tubercle bacillus from human sources.

The identity of tuberculosis as seen in man and cattle was held by Villemin, who believed he had proved the correctness of this view in his inoculation experiments, by which he showed conclusively that small animals like rabbits became tuberculous following the injection of material from man as well as cattle. Chauveau[5] was, however, the first to make the attempt to infect cattle with tubercular material from man, and his success is shown in the following abstract of his experiments:

FIRST SERIES. *Infection by the digestive tract.* Three animals were used, and as controls there were three other similar animals which were infected with bovine material, and also three which were not infected at all, these last remaining free from tuberculosis. Those to which bovine material had been fed as well as those which received human material became tuberculous. At the autopsy it was impossible to distinguish one set from the other. In all of them the lesions provoked showed the same character. The individual histories of the three animals infected with human material are as follows:

1. A heifer, six months old, which received material from the lung of a young man dead of acute miliary tuberculosis. Two doses of an emulsion of this material were given morning and evening of the same day. It was killed on the fifty-seventh day, having lost flesh to a slight degree. The lesions were found almost exclusively in the abdominal cavity. In the small intestine there were more than two hundred tubercles varying from the size of a pea to that of the head of a pin. The liver contained upward of a dozen small tubercular masses on its surface. The peritoneum showed a marked eruption of tubercles.

2. A heifer, eleven months old, which received two feedings with an interval of two days, the material being taken in part from the lung of a child with acute miliary tuberculosis and in part from the lung of an adult with a marked chronic phthisis with caseation. The animal soon became sick, and during life tuberculosis could be detected. The submaxillary ganglion on the right side became enlarged about the fifteenth day, and increased steadily until the animal was killed on the fifty-ninth day. The intestinal tract was only slightly involved, but the ganglia related to the first portion of the digestive tract showed marked lesions. The right submaxillary and the retropharyngeal glands were considerably enlarged and showed a typical tuberculosis with some calcification. The principal lesions were found in the thoracic

cavity. In the lung were a dozen disseminated foci mostly superficial, most of which showed caseous points on section. Microscopical examination showed them to be made up of a great quantity of lymphoid cells, with some giant cells. In the neighborhood of these masses and also in areas far from them were found diffuse tubercles developing into the alveolar tissue, as well as in the perivascular and peribronchial connective tissue. These young lesions showed exactly the same histologic structures as the larger ones. The bronchial and mediastinal glands were also markedly involved.

3. A young bull, about ten months old, which received two feedings on two consecutive days, composed of an emulsion made from the lung of two persons who had died of chronic phthisis (caseous pneumonia). After a diarrhea, which lasted several days, the animal showed marked illness, and lost flesh. It soon began to cough, and so marked were the symptoms that it was slaughtered on the thirty-fourth day. In the small intestine there was a marked eruption of tubercles extending from about the second portion of the jejunum to the end of the ileum. In certain portions the mucous membrane was converted into confluent tubercles. The most interesting lesions were found on the mucous membrane of the respiratory tract. In the larynx and the upper part of the trachea were found masses of gray granulations, a few of which were red and ulcerated.

SECOND SERIES. *Infection by intravenous injection.* A calf, three months old, was inoculated into the jugular vein with 2 c.c. of an emulsion made from the lung of a child with acute miliary tuberculosis. It was killed on the twenty-ninth day. The lesions were confined to the chest, the bronchial and mediastinal ganglia showing the most marked changes. In the lung, on section, there were found well-marked gray granulations accumulated in the interior or around the small bronchi, which they sometimes occluded entirely. This was well seen with the naked eye, but was better demonstrated in microscopical sections.

THIRD SERIES. *Infection by subcutaneous inoculation.* Seven animals were inoculated. For three animals the material used was obtained from fungus masses from the joints in cases of white swelling; for three others from acute miliary tuberculosis, and in one from the lung of a horse which had developed a marked pulmonary tuberculosis due to the intravenous injection of material from the lung of a man. In all cases a tumor developed at the point of inoculation, which Chauveau describes as being a tuberculous tumor altogether typical. The neighboring glands showed always more or less involvement, but in no cases was there any general infection.

I have quoted these experiments at some length for the reason that they seem often to be overlooked, and for the further reason that they have recently been directly misquoted. Indeed, Koch himself said in his address before the British Congress on Tuberculosis, "If one studies the older literature of the subject, and collects the reports of the numerous experiments that were made in former times by Chauveau, Gunther and Harms, Bollinger, and others, who fed calves, swine, and goats with tubercular material, one finds that the animals that were fed with the milk and pieces of the lungs of tubercular cattle always fell ill of tuberculosis, whereas those that received human material with their food did not."

Bollinger,[6] in 1879, inoculated a young calf in the peritoneal cavity with material from a human lung. When killed after seven months the mesentery and peritoneal covering of the spleen presented a number of tumors from the size of a pea to that of a walnut, and which microscopically were identical with those found in pearly disease under natural conditions. The retroperitoneal and mesenteric glands were tuberculous also.

Klebs[7] caused a tuberculosis of the peritoneum identical with that which is seen under natural conditions by the intraperitoneal injection of human tubercular material. Kitt,[8] also, is quoted by Professor Johne as having had a similar result accompanied with generalized lesions following the intraperitoneal injection of the juice from a scrofulous gland taken from the neck of a man

Crookshank[9] injected tuberculous sputum into the peritoneal cavity of a calf, causing death on the forty-second day. The autopsy revealed extensive disease. "Extending over the mesentery from the point (inoculation) there were hundreds of wart-like, fleshy new-growths, some quite irregular in form, others spherical or button-shaped. There were similar deposits on the under surface of the liver, on the spleen, in the gastrosplenic omentum, and on the peritoneal surface of the diaphragm. On microscopic examination extremely minute tubercles were found disseminated throughout the lungs and liver. Tubercle bacilli were found in these organs and in the peritoneal deposits."

Sydney Martin[10] fed human tuberculous sputum to six calves. Four of these received each 70 c.c. mixed with their food at one meal. They were killed after 33, 63, 85, and 285 days. The first three showed respectively 53, 63, and 13 tubercular nodules in the intestine, while the fourth was entirely free. The two other calves were given 440 c.c. of sputum at one feeding. One was killed after fifty-six days, and showed tuberculosis of the intestine and mesenteric gland. The other was allowed to live 138 days, and was free from disease when killed.

At the recent Congress on Tuberculosis, Prof. Thomassen,[11] of Utrecht, reported the following experiment: A calf four weeks old was inoculated in the anterior chamber of the eye with a pure culture of the tubercle bacillus isolated from a case of tuberculous arthritis in man. An intense keratitis was set up, the cornea becoming so opaque that it was impossible to observe the alterations in the iris. It was killed after six weeks, and was found to be the victim of a pretty well generalized tuberculosis. Both lungs contained numerous miliary tubercles and some gray fibrous tubercles of larger size. The path of infection from the eye to the lung was mapped out by the condition of the subparotideal, cervical, mediastinal, and bronchial lymph glands of the same side.

Nocard[12] states that by inoculation into the arachnoid cavity of a small amount of human tubercle bacilli a rapidly fatal tubercular meningitis is set up identical with that seen in children. A calf, five months old was thus inoculated by him on August 2, 1901, and died on the 28th of the same month, the pia mater being infiltrated with tubercles which proved virulent for guinea pigs.

On the same day Nocard injected into the jugular of a cow which had become much reduced by chronic diarrhea, but which was free from tuberculosis as shown by the tuberculin test, 1 c.c. of a suspension of human bacilli. She died September 4th, and showed a number of small foci, softened or caseous and extremely rich in tubercle bacilli. He considers that in this case the animal was so weakened by the pre-existing diarrhea that its normal resistance was largely destroyed.

de Jong,[13] as the result of a series of comparative inoculations of human and bovine tubercle bacilli, states that seven cattle, namely, two calves six months old, three steers two years old and one eighteen months, and one calf seven or eight months old, all became tuberculous by the injection of pure cultures of the human tubercle bacillus. In only one of the seven was the disease grave and wide-spread; in four the lesions were retrogressive, and in the two remaining ones progressive.

Arloing[14] reports the following recent experiments: Three cultures of human origin were used, one of which had been under cultivation since 1896. With this culture a heifer, two years old, and a young calf were inoculated intravenously. The calf was killed after thirty-two days, and showed a typical eruption of minute tubercles all through both lungs, but especially marked in the anterior lobes. The heifer was kept for one hundred and twenty days, and was only slightly diseased, the lungs and pleuræ being involved. With the second culture, obtained from a case of pleurisy, a calf two and one-half months old was inoculated intravenously. Death ensued after seventeen days. The lungs alone were involved, showing many young nodules. The third culture was isolated from a case of pleuropericarditis, with involvement of the lungs, and with this a young bull convalescent from aphthous fever was inoculated intravenously, death resulting in thirty-two days. The thoracic cavity was principally involved, the anterior and middle lobes containing nodules throughout, and some lobules of the posterior lobes also. The bronchial and esophageal glands were tremendously enlarged, weighing thirty-five kilograms.

It may be objected to many of these experiments that the tuberculosis resulting from the inoculation did not cause death nor even serious illness, and it is probable that some of the animals would have recovered entirely if allowed to live. Admitting freely the truth of this, it may be pointed out that under natural conditions many cattle infected with bovine tuberculosis will remain for years apparently in perfect health, so much so that detection of the disease is possible only by means of tuberculin. So, also, in man, many cases of tuberculosis run a benign course, or remain stationary for years, while not a few end in recovery. Yet in man and in animals these benign cases may take on an acute form and end in rapid death, owing to some intercurrent affection which lowers resistance or permits the engrafting of a secondary infection. No one would hold that because of the benign course of the disease in the first instance that true tuberculosis did not exist.

Transmission of tuberculosis to cattle from phthisical attendants. There are on record a few instances of cattle becoming infected with tuberculosis through the sputum of phthisical attendants. In several of these the evidence is so clear as to leave no doubt that cattle are at times infected in this manner. Such instances have been reported by Cozette,[15] Cliquet,[16] Huon,[17] director of the vaccine laboratory at Marseilles, and Bang.[18] In most of these cases the sputum was introduced into the digestive tract with the forage, as well as inhaled in the dry state, but in Huon's animal the infection seems to have been entirely through inhalation.

Experiments at the Laboratory of the State Live-stock Sanitary Board. I come now to speak of the work done at the laboratory of the State Live-stock Sanitary Board, the results of which you see illustrated in the specimens presented here for your inspection and study. I cannot but feel that these specimens possess an unusual interest and importance in the solution of a problem which is now engaging the attention of scientific men throughout the world, and which has been made the subject of special investigation by the governments of many countries. Our first successful attempt to infect cattle with human tuberculosis was made in 1898, when four calves of nearly the same age, four to five weeks old, received intraperitoneally 10 c.c. of human tuberculous sputum, from different sources, but in all cases containing a large number of bacilli. One showed no ill effects except a slight rise in temperature, and the autopsy was entirely negative.

Of the other three, two had persistent high temperature following the injection, but only one showed marked illness otherwise. Postmortem examination proved that all had become infected with tuberculosis, the lesions in two being quite extensive. I will give here the details of only the one which showed marked illness during life. The lesions were so extensive and typical that even the most skeptical must admit the success of the experiment, and I have here some of the organs for inspection.

Calf No. 8050, aged four weeks, was inoculated on May 16, 1898, with sputum from an early case of pulmonary tuberculosis at the University Hospital. The sputum contained a large number of tubercle bacilli. Soon after the operation the temperature of the calf rose and continued high, with some remissions, until it was killed. Its appearance was bad, the coat dry and rough, the respiration rapid. It was tested with tuberculin, but the temperature was too high for results. It was killed on August 1st, weighing 190 pounds. On the surface of both lungs there was a slight deposit of fibrin, and on section a number of hemorrhagic areas were observed in both. The mediastinal and bronchial glands were enlarged and congested. The abdominal cavity contained about 12 ounces of bloody serum. The peritoneum was thickly studded over its entire surface with nodules from 1 mm. to 12 mm. in diameter, fibrous in character. In many places these nodules had massed together, forming tumors, some 5 cm. in diameter, which were dense and fibrous. The spleen contained many nodules, both on its surface and throughout its substance. The whole omentum was thickly studded with nodules from 2 mm. to 12 mm. in diameter, and besides which there were three large masses, dense and fibrous in character, two of which were 15 cm. long by 7 cm. wide, and 12 mm. thick; and the third 7 cm. long by 6 cm. wide, by 4 cm. thick. The abdominal surface of the diaphragm was thickly studded with nodules, fibrous in character. The mesentery was thickened and contained many nodules of small size. The appearance was that of a typical case of grape or pearl disease. The mesenteric and mediastinal glands were enlarged and somewhat caseous.

For several years past we have endeavored to obtain material from cases of tuberculosis in children in which there was evidence of infection through the alimentary tract, reasoning that if children contracted tuberculosis through the ingestion of milk from diseased cattle we would be most apt to find bacilli of the bovine type in these intestinal or mesenteric lesions. So far only three such cases have come to us, all through the kindly interest of Dr. Alfred Hand, and in only one of these was the evidence of primary intestinal infection clear. We have isolated from the mesenteric gland of this child, the immediate cause of whose death was tubercular meningitis, a culture which has for cattle the most intense pathogenic power. Two calves inoculated into the jugular vein and peritoneal cavity died in nineteen and twenty-seven days respectively; and a grown cow which was inoculated both in the jugular vein and peritoneal cavity died in eighteen days. All of these animals exhibited marked symptoms from the day of inoculation. Examination of the lesions, both macroscopic and microscopic, leaves no doubt that the animals succumbed to a pure tuberculosis. The details of these cases are as follows:

History of culture. Designation BB. Obtained from a child seventeen months old. Death was due to tubercular meningitis. Autopsy: Lungs normal, except posterior part of the right upper lobe, which was consolidated, red on section, and had excess of connective tissue. Bronchial and mediastinal glands not enlarged. Spleen, liver, and kidneys show pearly tubercles. Two feet from lower end of ileum is an ulcer 1 cm. by 2 cm., the long diameter transverse to axis or gut. Nodules are seen on peritoneal surface. Four small ulcers, two above and two below, are found in ileum. Mesenteric glands enlarged, cheesy, and some purulent. Meninges show yellow tubercles most marked along longitudinal fissure, in choroid plexus and over cerebellum. The mesenteric glands were used in obtaining the culture.

This case is considered by Dr. Hand the clearest one of primary intestinal tuberculosis ever seen by him.

Guinea-pigs were inoculated intraperitoneally with an emulsion made from the mesenteric glands on March 9, 1901. One was chloroformed on April 19th, and cultures made. Scanty growth on one tube was found on June 8th, and subcultures made.

Calf No. 26596, weight 132 pounds. Tested with tuberculin, but gave no reaction. On December 4, 1901, 5 c.c. of a suspension of the fifth and sixth generation of Culture BB were injected into the right jugular vein. On the next day the temperature had risen to 103.2 F. After a slight remission it rose to 103° F. on the seventh day after inoculation, and continued to rise each day, reaching 106.4° F. by the fourteenth day, after which it fell slightly until death, which took place on December 21st, seventeen days after inoculation. The animal showed marked illness during life, the respiration reaching 68 per minute.

Autopsy. The lungs and the related glands showed macroscopically the most marked disease. Both lungs were thickly studded throughout, with remarkable uniformity, with miliary nodules, giving a sandy feel under the finger. The left was pneumonic, owing to the position of the calf for some time before death. Portions of the right were in a similar condition, sinking when placed in water. The bronchial and mediastinal glands were much enlarged and soft, and in the former small areas of caseation were found.

The liver was large, soft, and friable. Several nodules were visible on the surface, though not perceptible to the touch. The spleen showed very slight changes. The kidneys were normal.

Calf No. 26597, weight 202 pounds. Tested with tuberculin, and gave no reaction. On December 4, 1901, 5 c.c. of a suspension of Culture BB of the fifth and sixth generations were injected into the peritoneal cavity. The temperature rose to 105.2° F. by the eighth day after injection, remaining very nearly the same until four days before death, when it began to fall, and reached 103° F. on the day before death, which took place on December 31st, or twenty-seven days from the time of inoculation.

Autopsy. Great emaciation. Loss in weight thirty-seven pounds. The lungs were largely involved, though not uniformly. The central and posterior portions showed many areas deep red in color and solid to the feel. These were thickly studded throughout with minute grayish nodules.

The suprasternal lymph glands were as large as goose eggs, and contained cheesy areas. The mediastinal glands were much enlarged, one being six inches in length by two inches in diameter. The peritoneal cavity contained about six quarts of straw-colored fluid. The peritoneum was everywhere enormously thickened, and practically converted into a tuberculous mass. In several places it was one-half an inch thick and fibrous. The omentum was also enormously thickened and bound over the surface of the liver. It contained a great number of nodules, dense and fibrous, many with caseous centers. The liver was firmly adherent to the diaphragm, and on section showed many nodules. The spleen was firmly attached to the surrounding parts by a mass of partly organized fibrin, which contained many cheesy nodules. On section it appeared to be normal.

Cow No. 45030, about three years old, and weighing 660 pounds. On January 22, 1902, 2½ c.c. of a suspension of Culture BB of the seventh and eighth generations were injected into the right jugular vein and the same amount into the peritoneal cavity. The temperature rose to 103.2° F. on the second day, then fell slightly during the next six days, after which it rose steadily, reaching the maximum, 107° F., three days before death, after which it fell slightly, the animal dying seventeen days after inoculation. The lungs were mostly involved, both being thickly studded throughout with miliary nodules. Most of the left lung showed interlobular emphysema, while the inferior portion was much congested. On the omentum were numerous dark red spots which could be felt between the fingers. The spleen was adherent to the diaphragm, and there were many punctate hemorrhages on the surface. The liver and kidneys showed no gross changes.

What interpretation is to be given to these remarkable results? One of two propositions must be admitted: either we have found a human tubercle bacillus having a pathogenic power for cattle quite as great as any bovine germ, or else we have found in the mesenteric gland of a child the bovine tubercle bacillus. If we accept the law of diagnosis laid down by Koch, namely, the inoculation test, the latter is the true explanation. I, myself, am strongly of the opinion that this latter is the case for the following reasons:

1. The history of the case as given by Dr. Hand, primary intestinal infection.

2. Morphologically and culturally the organism corresponds more nearly to the bovine type as first defined by Dr. Theobald Smith, and later by ourselves, than the human.

3. The great pathogenic power for cattle.

A second culture obtained from the mesenteric glands of a child has shown a virulence far in excess of that usually found in human cultures, though it falls short of Culture BB in pathogenic power. This culture, designated U, was isolated in December, 1900, and tested for guinea-pigs and rabbits. The results, together with its manner of growing and microscopic appearance, led us to consider it a typical human culture. During the summer of 1901 it was selected for some feeding experiments on puppies, and showed a degree of virulence that was not expected. In December last, wishing to produce a slow tuberculosis in a dog, this culture was again employed. The dog grew ill rapidly, and died in January, thirty-six days from the time of inoculation. Post-mortem examination revealed a typical and extensive tuberculosis, and it was decided to inoculate a calf in order to test its virulence for the bovine race. On March 4, 1902, Calf No. A45046, weighing 74 pounds, was inoculated in the jugular vein with 6 c.c. of a suspension of Culture U, of the twelfth generation, from glycerin-agar, the suspension being equal in opacity to a twenty-four-hour-old culture of the typhoid bacillus in bouillon. The animal soon showed signs of illness, the breathing became rapid and labored, reaching 54 per minute. Extreme weakness and depression came on, and it passed much of the time lying down. On April 19, 1902, it was killed, death seeming imminent.

Autopsy. Weight 82 pounds. Condition fair. The anterior lobes of both lungs were thickly studded with minute nodules, averaging 1 mm. in diameter. Blocks from these lobes sank in water immediately. Both lungs were dense and solid to the feel throughout. The posterior lobes were air-bearing for the most part, but contained many solidified areas, which could be seen on the surface as well as on section.

The bronchial and mediastinal glands were enlarged and wet. Scrapings from cut surfaces show an enormous number of tubercle bacilli. In the mediastinal glands many yellowish nodules were seen. The pleuræ were normal. The liver was enlarged and firm to the touch. No distinct nodules could be seen by the naked eye, but throughout the substance yellowish areas were found in large numbers. The surface appeared marbled.

The spleen was enlarged and very firm, but no nodules could be detected. The kidneys showed numerous whitish areas on the surface, which were found to extend quite deeply into the cortex. On section many yellowish nodules were seen. The tissues of the kidneys were much stained with bile, and the pelvis contained a gelatinous or viscous material showing the same pigment. The peritoneum was normal.

Microscopic examination. The solidified portions of the lungs contained large areas which are not air-bearing, the alveoli being completely filled with leukocytes and epithelium, or epithelioid cells. The small bronchi are filled by an exudate made up largely of leukocytes. The central portions of the nodules stain poorly, and fragmentation of the nuclei of the cells is seen, but no distinct caseation can be found. In sections stained with carbol-fuchsin innumerable tubercle bacilli are seen. In other parts of the lungs which are still largely air-bearing, minute nodules are found in large numbers having the same general characteristics as those just described. Throughout the sections many tubercle bacilli are seen, and in the nodules they are in clusters. In the liver no typical tubercles are found, but there are many minute nodules made up of round cells, and on the borders of these a considerable number of giant cells with peripheral nuclei occur. Sections stained with carbol-fuchsin show large numbers of tubercle bacilli clustered in these areas.

The spleen shows round-cell infiltration, giant cells, and many tubercle bacilli.

The white areas in the kidney described above show a round-cell infiltration and large numbers of tubercle bacilli. The bronchial glands show areas of beginning caseation, a few giant cells, and innumerable tubercle bacilli.

This calf showed a well-marked tuberculosis, proving that the culture with which it was inoculated had a degree of virulence above that usually found in cultures of human origin. Our experience with this culture leads us to believe that the usual method of employing only guinea-pigs and rabbits in testing the virulence of the tubercle bacillus does not always give entirely conclusive results. Unfortunately, the expense attending the use of larger animals hinders their more general employment.

History of Culture U. Obtained from a child, aged three years, whose death was due to tubercular meningitis. Autopsy: Lungs and bronchial lymphatic glands full of miliary tubercles. Anterior mediastinal glands much enlarged. Spleen extensively involved, liver less so. On the abdominal surface of the diaphragm were a number of flat, yellow nodules. Mesenteric glands enlarged, and contained old, yellow, cheesy nodules. One small tubercle found in the right suprarenal. Purulent and cheesy nodules found in meninges and encephalon. The cultures were obtained from the mesenteric glands.

The pathologist, Dr. Hand, was unable to decide with certainty as to the origin of this case.

Increase of virulence by successive passages through calves. In another experiment instituted by Dr. Leonard Pearson we have proved that a typical tuberculosis can be produced in young cattle by large and repeated doses of a human culture of moderate virulence; and what is even more interesting and important, by successive passages through calves we have succeeded in bringing about a marked increase in the virulence of this culture. The culture employed was isolated from human sputum in September, 1899, and is designated "M."[4] The animals were inoculated at intervals of a week, the amount of culture being divided into four equal portions, which were injected into the jugular vein, the lung, the peritoneal cavity, and under the skin. Each week the dose was increased by 10 c.c.

Two calves were infected in this manner, Nos. 26562 and 26563. With the tissues of No. 26562 the serial inoculations were begun, the details of which, with the postmortem examination of the animals, is given below. The result is shown in the following table:

No.	*Amount of Injection.*	*Length of Life.*
1. Calf 26562	925 c.c.	106 days,
2. " A45020	16 "	48 "
3. " A45035	13 "	23 "
4. " A35047	10 "	24 "
5. " A45073	14 "	24 "

Calf No. 26562, weight 210 pounds. The first inoculation was made on September 6, 1901, and thereafter at intervals of a week, until December 16th. Each time the total amount was divided into four equal parts and injected subcutaneously, intraperitoneally, into the lung, and into the jugular vein. The commencing dose was 10 c.c. of an emulsion equal in opacity to a twenty-four-hour-old bouillon culture of the typhoid bacillus, the total amount given being 925 c.c. The temperature rose after each injection, and remained high for two days, then fell gradually, though normal was never reached. About five weeks after the first injection the the calf began to cough. This cough grew steadily worse until death, being most marked on the day following each injection. Respiration grew labored, and the animal lost flesh. By December 15th it was markedly ill. Death took place during the night of December 21st.

Autopsy. Considerable emaciation. The lungs were hard and firm to the touch. The various sites of inoculation could not be detected, and there were no abscess cavities nor scars. The lungs were dense throughout and heavy, though sections floated in water. The bronchi, especially the smaller ones, were filled with a tenacious mucus, in which many tubercle bacilli were found. An emulsion made from one of them showed many tubercle bacilli. The mediastinal glands were large and soggy, but no nodules could be found. The bronchial glands were enlarged, and a few caseous points were found. An emulsion made from one of them showed many tubercle bacilli. The mediastinal glands were large and soggy, but no nodules could be found. The liver was attached to its capsule at points which were the sites of flat, yellowish nodules, from 2 mm. to 5 mm. in diameter. On section tuberculous areas of considerable extent were found, reaching from the surface to a depth of 3 cm. The spleen was much enlarged and very soft. On the surface were a number of flat fibrous new-growths. The kidneys showed no changes. The omentum was much discolored, having a dirty, brownish appearance, and in parts much thickened. It contained upward of 100 nodules of 2 mm. to 6 mm. in diameter, some gray, some white, and some hemorrhagic. Some had the appearance of beginning "grape" formation. The mesentery presented the same appearance. Its glands were enlarged and wet, but no cheesy nodules could be found. On the parietal peritoneum were a large number of pearly nodules, 2 mm. in diameter, and a few sessile new-growths, some of which were hemorrhagic, and had fringes of fibrin hanging from them. Microscopic examination of the tissues showed the spleen and kidneys to be free of tubercles. In the lungs the greater part of both is made up of conglomerated tubercles which show very little central caseation. The alveoli are completely filled with desquamated epithelium, leukocytes, and epithelioid cells. There is a marked bronchitis.

Calf No. 26563, weight 165 pounds. The first inoculation was made on September 6, 1901, and thereafter weekly until December 16, 1901, when an interval of nineteen days was allowed to elapse, the inoculations being resumed on January 4, 1902. The method of inoculation was the same as for Calf No. 26562. Death took place January 22, 1902, the total amount of the suspension of the culture given being 1400 c.c. The condition of the animal following the injections correspond closely with Calf No. 26562, its survival being somewhat more prolonged.

Autopsy. Weight 186 pounds. Considerable emaciation. The lungs were firm and non-elastic to the touch. The points of inoculation could not be detected either in the pleuræ or in the lungs, except at one point, where a small pus cavity, 1 cm., was found near the surface of the right lung, the pus containing many tubercle bacilli. No distinct nodules could be found in either lung, but both were much increased in solidity throughout, though sections would float in water. The bronchi were filled with a tenacious mucus. The pleuræ were roughened by bands of fibrin, which extended to the lung, attaching the inferior borders especially to the chest-wall. The bronchial and mediastinal glands were much enlarged, and the latter contained many caseous nodules. In the abdominal cavity all the organs were attached to the peritoneum and to each other by bands of fibrin. The liver was firmly adherent to the diaphragm. Over the surface were fifty to sixty whitish, flat nodules, 5 mm. to 10 mm. in diameter, some of them extending deeply into the substance of the organ. On section caseous areas were seen.

The spleen and kidneys showed slight changes only. The parietal peritoneum was rough at many points and had fringes of fibrin attached to it. Scattered over it were a large number of gray nodules, 2 mm. to 5 mm. in diameter.

Microscopic examination showed no well-defined tubercles in the spleen and kidneys. The liver showed many areas of necrosis. In the lungs were masses of conglomerated nodules, most of which did not show marked central caseation. Numerous giant cells were found. The alveoli are filled with desquamated epithelium, leukocytes, and epithelioid cells. There is a marked bronchitis.

Calf No. 45020, six months old. On December 23, 1901, 8 c.c. of an emulsion made from the bronchial gland of Calf No. 26562 were injected into the left lung, and the same amount into the peritoneal cavity. The emulsion showed many tubercle bacilli. By January 15, 1902, the calf was markedly ill, and breathing was increased in rapidity. These symptoms increased steadily, the temperature ranging from 104° F. to 105.5° F. About February 1st the temperature began to fall, and at the time of death, February 9th, was subnormal.

Autopsy. Much emaciated. Both lungs were a dark red, and were thickly sown throughout with miliary nodules. The left lung was adherent to the chest-wall over a large part of its surface. On separating it many tubercular new-growths were seen, between which the pleura was smooth. At the point of inoculation was an abscess cavity 4 cm. in diameter. The pus contained many tubercle bacilli and staphylococci. On the lung over the abscess, and binding it lightly to the chest-wall, was a layer of fibrin, of cream-white color. Along the backbone was a chain of enormously enlarged glands fitting into the spaces between the ribs, and extending from the first rib to the diaphragm. These were filled with caseous areas. The mediastinal glands were enlarged and showed many caseous areas. Most striking was the condition of the omentum, which had been converted into a mass of tubercular new-growth, made up of conglomerate nodules. It varies in thickness from 1 cm. to 3 cm. The nodules are grayish-yellow, fibrous, and show central caseation. The liver shows numerous yellowish nodules, both on the surface and on section.

The spleen has on its surface a number of flat, fibrous new-growths, but no nodules are seen on section.

The kidneys are normal in appearance, but a few nodules appear on section.

Microscopic examination shows the lungs to be thickly sown with minute tubercles. Sections stained with carbol-fuchsin show innumerable tubercle bacilli clustered mainly in these nodules.

The liver contains many necrotic areas in which many tubercle bacilli are found. The spleen contains a considerable number of necrotic areas. The flat new-growths are tuberculous. The kidneys show only a few tubercles, which contain innumerable tubercle bacilli.

Calf No. 45035, aged nine weeks, weight 130 pounds. February 11, 1902, inoculated into its right lung and peritoneal cavity with an emulsion made from the omentum of Calf No. 45020, 5 c.c. being injected into the lung, and 8 c.c. into the peritoneal cavity. The temperature rose on the day after the inoculation, and reached 107° F. on the third day, after which it fell, and ranged from 104° F. to 106° F. until a few days before death, when it fell slightly, going as low as 101.4° F. on the day of death. Breathing had become labored ten days before death, and the appetite failed a week before death, which took place March 6th.

Autopsy. Weight, 97 pounds. Condition fair. The right lung adherent to chest-wall throughout. When separated a layer of fibrin containing many tubercular masses of new-growth is seen. At the point of inoculation is an abscess cavity 4 cm. in diameter, the pus containing many tubercle bacilli and a gas-forming bacillus of the colon group. Both lungs were filled with a multitude of minute nodules, and some areas showed extensive caseation. The mediastinal and bronchial glands were very much enlarged and caseous.

The liver, spleen, and kidneys were normal in appearance.

The omentum contained a very large number of discolored, reddish areas, which were thickened, hard, and of sandy feeling.

Microscopic examination. The lungs are studded with minute tubercles. The liver contains many small areas of necrosis. The spleen shows a number of areas of commencing necrosis. The kidneys are normal.

Calf No. 45047, aged six weeks, weight 72 pounds. Inoculated March 7, 1902, with an emulsion made from the lung and bronchial gland of Calf No. 45035, 5 c.c. being injected into the right lung, and 5 c.c. into the peritoneal cavity. The temperature rose to 104.8° F. to 106° F. for ten days, then fell slightly until death took place, on April 1, 1902.

Autopsy. Weight 65 pounds. Considerable emaciation. Both lungs are studded throughout with miliary nodules. The right lung is firmly attached to the chest-wall for its entire surface, and at the point of inoculation is an abscess 4 cm. in diameter, which contains a milky fluid pus in which are curdy masses. The pus contains many tubercle bacilli and other bacteria, but no streptococci. The left lung is attached to the chest-wall for a third of its surface. Over the unattached surface is a layer of fibrin, 1 mm. in thickness. The chest-wall corresponding to this fibrin is thickly studded with minute gray nodules. The pericardium is attached to the lung. The heart shows numerous yellowish tubercles scattered over the ventricles, as well as the auricles, and especially numerous on the auricular appendage. They are seated in the visceral layer of the pericardium.

The bronchial and mediastinal glands are enlarged and soggy, but no nodules can be found.

The omentum contains innumerable minute pearly nodules, and many red, fleshy, highly vascular new-growths.

The mesentery of the large as well as small intestine contains innumerable pearly nodules. The mesenteric glands are normal in size and appearance. Along the abdominal aorta and brim of the pelvis are twelve to fifteen glands from 5 mm. to 15 mm. in diameter, yellow in color, but none caseous.

The liver is adherent to the diaphragm. On the surface, as well as on section, many yellowish nodules can be seen.

The spleen is thicker than normal and very firm. On the surface a few fibrous new-growths are seen.

The kidneys appear normal, but each has a layer of the peritoneum attached to it, which contains innumerable gray nodules, averaging 1 mm. in diameter.

Microscopic examination. Lung not examined. The liver contained many minute areas of necrosis. The kidneys contain a considerable number of minute tubercles, with central necrosis, situated for the most part immediately under the capsule.

Another animal was inoculated in the same manner with the tissues of this calf, which is still living.* Guinea-pigs have also been inoculated in order to recover a pure culture, so that any changes that have taken place may be studied. We feel, however, that we have demonstrated a great increase in virulence in this culture, obtained from sputum, by the several passages through calves.

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* This calf, No. A45073, died three days after the reading of the paper, or twenty-four days after inoculation. There was typical and extensive tuberculosis.

Our own experiments, as well as those quoted from others, demonstrate that Koch's statement that human tuberculosis cannot be transmitted to cattle is erroneous and untenable.

II. In the second proposition Professor Koch calls in question the possibility of the transmission of tuberculosis from cattle to man, and holds that if such transmission ever does take place it is a very rare occurrence, so rare, indeed, as to render superfluous any measures of precaution against it.

In the solution of the problems here involved we are of necessity deprived of experimental data, so must gather evidence from every possible source, collate and weigh it carefully, in order to draw fair conclusions.

In the first place, we may well ask if tuberculosis in cattle is marked by any specific features which differentiate it from tuberculosis in man, and which would make it improbable that the two were intercommunicable. I will not attempt here to go into a discussion of all the forms of bovine tuberculosis or to compare it minutely with the disease in man. The chief differences are: (1) The marked tendency to calcification rather than the caseation seen in man; (2) the formation of extensive new-growths in the serous membranes, such as the pleuræ and peritoneum.

These growths assume wart-like, or cauliflower, or grape-like shapes, from which the names "perlsucht," "pearly disease," "pommelière," and "grape disease," as applied to bovine tuberculosis, are derived.

In cattle, as in man, the lungs are the chief seat of the disease. In about half of all cases the lungs and serous membranes are simultaneously affected; the lungs alone in about one-third, and the serous membrane alone in about one-fifth.

Since 1863 Virchow[19] has insisted that the two tuberculoses were distinct, an attitude reaffirmed by him in his latest publication, his chief point being that we cannot call anything tuberculosis which does not show the true histologic tubercle, whether or not the tissues contain tubercle bacilli and show changes due entirely to them. Although insisting so strongly on this distinction, which is not held by all pathologists, Virchow does not accept Koch's conclusions, and says that in the postmortem examinations at the Charité several cases have been found showing an unusual peritoneal tuberculosis, with enormous growths, such as are seldom seen in man. These cases he regards as being possibly of bovine origin through food.

The histologic identity of human tuberculosis and pearl disease was first demonstrated by Schüppel,[20] and his work has been supplemented by Baumgarten,[21] who has observed characteristic caseation such as occurs in the human tubercle, take place in the nodules of pearl disease, "in a typical form and with like regularity." The process is often obscured by rapid calcareous changes which, he justly remarks, are terminal, and have nothing to do with the actual disease, and which, furthermore, are often seen in human tuberculosis. On the other hand, it has repeatedly been shown that typical miliary tuberculosis can be produced in cattle by the bovine bacillus, and as seen in the specimens before you the same result may be brought about at times by the human bacillus. In fact, experimental tuberculosis in cattle induced by inoculation with the bovine tubercle bacillus is usually of the miliary type, and only exceptionally assumes the form considered typical of the natural bovine disease. In this connection Hueppe[22] very aptly calls attention to the fact that Koch in his experiments with the bacilli of bovine tuberculosis produced in cattle "only tuberculosis, but not the tuberculosis of the pleura peculiar to the ox—the so-called perlsucht; his experiments, therefore, in the sense of his special interpretation, did not even prove that bovine tuberculosis affects the ox." It has further been shown by Troje,[23] and by Dr. Theobald Smith,[2] that pearl disease may be produced in rabbits by the human tubercle bacillus. Troje has observed one case of pearly disease affecting the pleura in man.

The differences noted between tuberculosis of man and tuberculosis of cattle are scarcely greater than those noted between the latter and tuberculosis of swine, yet nothing is easier than to infect swine with the milk or other products of tuberculous cattle. The infection here is by natural methods, and in fact is most often noted where nothing was further from the wishes or intentions of the unconscious experimenter. The origin of the infection is unquestionably bovine, yet the disease produced differs markedly, but not essentially, from that seen in cattle. The evidence then leads us to conclude that such differences as are commonly seen between human and bovine tuberculosis are in no sense essential.

Bacteriologic evidence. Morphology and cultural characteristics of human and bovine tubercle bacilli. That there were certain differences to be observed in cultures of the tubercle bacillus isolated from man and from cattle was shown by Dr. Theobald Smith in 1896, who confirmed his first observations in 1898, his human cultures being almost always obtained from sputum. A study similar to Dr. Smith's has been carried on at the laboratory of the State Live-stock Sanitary Board of Pennsylvania for several years, the material for the cultures being obtained from divers sources. With one exception, which was isolated from sputum, all the human cultures have been obtained from internal organs, especially the lungs and mesenteric glands. Two of the bovine cultures have been found in milk, the others coming from internal organs or glands. The result of our observations, which have agreed closely with those of Dr. Smith, is as follows: The morphology of the bacilli in cultures of bovine origin is more uniform and constant than in cultures from man. The bovine bacilli are thick, straight, and short, seldom more than 2μ in length, and averaging less. In the early generations many individuals are seen which are oval, their length not more than double their breadth. They stain evenly and deeply with carbol-fuchsin, beading being almost always absent from young cultures and often from old ones.

The human bacilli are, as a rule, much longer from the start, and tend to increase in length at once in sub-cultures. They are generally more or less curved, some cultures showing S-shaped forms. They stain less intensely with carbol-fuchsin, and beading is generally seen, even in early growths.

The above characteristics are most marked and most persistent in cultures grown on blood-serum. On glycerin agar, glycerin bouillon, and glycerin potato the bacilli from the two sources approach each other in cultural features and morphology much more closely, and by continued cultivation the differences tend to become obliterated. Bovine cultures are more difficult to isolate than human, are apt to grow as discrete colonies in the first culture, and for several generations are likely to grow in an exceedingly thin layer which resembles ground glass closely. The optimum temperature as well as the thermal death-point are practically the same.

The human bacillus, as a rule, grows more easily and abundantly from the first, and will grow well on glycerin agar in sub-cultures made directly from the original growth on blood-serum. All attempts to obtain a like result with the bovine organisms have failed.

The morphologic distinctions tend to disappear also in the tissues of susceptible animals. We may inoculate a typical bovine culture, and in a very short time scrapings from the various organs will show long and very much beaded bacilli.

The most striking dissimilarity is, however, seen in the action of the bacilli from the two sources on animals. By whatever method of inoculation, the bovine bacillus, as a rule, possesses a very much greater pathogenic power than the human bacillus for all animals on which it has been tried, the only exceptions being possibly those animals, like guinea-pigs and swine, which are so extremely susceptible to both types that it is hard to draw any distinction between them. This was the case with swine inoculated by feeding in our own experiments, but Koch and Schütz found that for swine also the bovine bacillus was much more active. The list of animals for which this increased virulence has been proven includes horses, cows, asses, sheep, goats, dogs, cats, rabbits, guinea-pigs, and recently the same thing has been shown to hold true for man's relative, the monkey, by de Jong,[13] de Schweinitz and Schroeder,[24] and ourselves.

In our own experiments two monkeys inoculated subcutaneously with Culture L, obtained from milk, died on the thirty-seventh and thirty-third days, while the corresponding pair of the same species, and as nearly the same weight as possible, inoculated with Culture M, from human sputum, lived fifty-four and ninety-six days, respectively, the last being chloroformed in a moribund condition. Two other monkeys which were inoculated by feeding five times with the same cultures smeared on banana, lived forty-two and ninety days, respectively. The postmortem examinations showed for the animals which received the bovine cultures a more active invasion and more acute process.

What has been said concerning the greater pathogenic power of the bovine organism has, I think, been proven beyond question to be the rule. It must be borne in mind, however, that what we speak of as virulence is a very variable quantity, no micro-organism being known which always shows the same degree of pathogenicity. The tubercle bacillus isolated from cattle varies in its pathogenic power considerably, though not perhaps to such an extent as those obtained from human sources. Among the latter we find some cultures which have feeble action even on the most susceptible animals, like guinea-pigs,[25] while others are most actively virulent. Besides Culture BB, described in this paper, cultures of exalted virulence have been isolated from man by Vagades[26] and Lartigau.[27] Whether or not these cultures were in reality the bovine organism which had infected man we cannot say now. At present our knowledge is so restricted in the matter of differentiation that we must designate the cultures human or bovine according as they are isolated from man or from cattle. The dictum of Koch that inoculation of cattle will infallibly distinguish one from the other cannot be accepted offhand, as it is far from proven that virulence for cattle is a fixed and constant characteristic. Prof. McFadyean[28] says: "If a low degree of virulence for cattle is to be taken as the distinguishing feature of human bacilli there will be no difficulty in proving that human disease is sometimes transmitted to the lower animals."

Has the bovine tubercle bacillus more pathogenic power for man than the human bacillus? In trying to interpret the results obtained by inoculation of animals we are forced to ask ourselves whether or not they are applicable to man also? Having proven that for practically all experimental animals the bovine tubercle bacillus possesses, as a rule, a much greater pathogenic activity than the human, is it fair to conclude that this increase of virulence will hold good for man also? Until the contrary is proven, or until good reason for believing the contrary is shown, I feel that this must be our conclusion. This matter opens up a most fascinating field for speculation, in which we meet with many apparent contradictions; and until we gain a better understanding of immunity in general we cannot speak dogmatically, but must stick to ascertained facts in each individual case. Virulence is a factor which is relative to the subject, and exaltation of virulence for one species of animal does not necessarily prove an increased power for other species. Indeed, the reverse is sometimes true. For example, the streptococcus is said to become increased in virulence for mice by successive passages through these animals, but less virulent for rabbits. So, too, the bacillus of "rouget du porc," though but slightly pathogenic for rabbits, rapidly acquires a high degree of virulence for them by successive passages; but when this has taken place we find that all virulence for swine, from which it came in the first place, has disappeared. Large doses do not even make them ill.

Admitting freely all these facts, we must regard them as exceptional, for it is a firmly established rule in bacteriology that when the virulence of a pathogenic organism is increased for one animal it is increased for all that are naturally susceptible to its action as well as for those in which the disease is known only experimentally.

That as regards man a result analogous to that seen in the streptococcus, or the bacillus of "rouget du porc," has not taken place by the residence of the tubercle bacillus in the tissues of cattle is proven by the cases of accidental inoculation of man with the bovine bacillus as well as by the cases observed clinically in which tuberculosis has followed the consumption of tuberculous milk. The tubercle bacillus is unique in the extent of its pathogenic activity, both by direct experimental inoculation as well as by infection under what may be considered more or less natural conditions. The list of animals in which tuberculosis occurs in parks and zoological gardens is appalling, the discoveries of Dubard[29] and others showing that not even the cold-blooded animals are exempt from this universal scourge. While it may be said of the tubercle bacillus that in cultures in the laboratory it is unusually tenacious of its characteristics, it is certain that in nature it has a wide range of adaptability as a pathogenic agent. Hence, for the tubercle bacillus, perhaps, more than for any other known microbe, we are justified in believing that an exaltation of virulence for practically all experimental animals will hold good in the case of man also.

Accidental inoculation of man with the bovine tubercle bacillus. While we cannot determine the virulence of the bovine tubercle bacillus for man by direct inoculation, we are, nevertheless, not without some information on this point, owing to the accidental inoculations observed from time to time. Four such cases have been reported to this Society, accompanied in three instances by the exhibition of the specimens.[30]

Similar cases have been reported by Tscherning[31] and Pfeiffer,[32] the latter ending in general infection and death.

Dr. M. B. Hartzell[33] has also observed two cases in which the bovine origin of the infection was not absolutely proven, though certainly highly probable, both occurring in healthy men who were employed by one of our large railways to clean and repair cattle cars. In both a well-marked tuberculosis of the skin of the verrucous type followed slight wounds of the back of the hand inflicted by broken timbers. One man recovered under local treatment, but the other died after about a year through involvement of the lungs and other organs. This patient was a robust man, aged forty-four years, weighing 175 pounds, with good personal and family histories. Dr. Hartzell felt that he was able to exclude with reasonable certainty any other source of infection. The death of Mr. Thomas Wally, Principal of the Royal Veterinary College of Edinburgh, is also attributed to infection gaining entrance through a wound received while making an autopsy on a tuberculous cow.

The interest which has been aroused by Professor Koch's paper has brought out numerous reports of such cases, which are now being published to show that man has something to fear from bovine tuberculosis.

Dr. Kurt Mueller,[34] a surgeon of Erfort, describes the cases of two healthy young men who were under his care. Both were butchers, and in both cuts were sustained while working on tuberculous cattle, the wound opening the synovial sheath of a tendon in the hand. In each case an operation was necessary, and it was found that the wall of the sheath, as well as the tendon itself, was thickened, while upon them were large numbers of yellow nodules, proven to be tubercles by microscopic examination. These tubercles were placed very thickly near the scar, gradually becoming fewer as the scar was left. In one of the men the trouble extended from the finger to the forearm, and there was some evidence of tuberculosis even at the muscular attachment of the tendon. In the second case the tendon was attached to the sheath, and the disease limited to an area 10 cm. in length. Examination of the removed tissue proved the presence of tubercle bacilli. Both of these men had good family histories, and were free from tuberculosis elsewhere, so that Dr. Mueller has no doubt that they were inoculated with bovine tubercle bacilli.

de Jong[13] observed the case of a man who injured his finger while examining the mesentery of a tuberculous cow. The wound did not heal, the edges became indurated, and considerable swelling ensued, with pain which increased steadily and failed to yield to ordinary treatment. Curettage and cautery were finally used with success. In the scrapings tubercle bacilli were demonstrated.

In Berlin[35] two men who are employed in the slaughter-house to carry the condemned tuberculous meat to the place where it is destroyed have developed tuberculosis of the skin of the hands. At a recent meeting of the Medical Society of Berlin, Professor Lassar[36] presented cases of verrucous tuberculosis of the skin. He had observed this type of skin tuberculosis in butchers who had handled tuberculous meat. Of thirty-four cases seen by him four were in butchers; while, on the contrary, among those affected with other forms of tuberculosis localized to the skin of the hands, none belonged to this calling. Liebreich agreed with the view taken, and said he had been able to assure himself that verrucous tuberculosis of the skin was much more common among those whose duties require handling tuberculous meats than among others. Blaschko spoke of the case of a cook seen by him in whom a tuberculous lesion followed the prick of a piece of bone.

It is interesting to note that Dr. Hartzell's two cases were both of the verrucous variety, the origin in both having been almost certainly bovine.

Drs. Joseph and Trautmann[37] report three cases of verrucous tuberculosis of the skin occurring among employes of the municipal abattoir in Berlin, who worked exclusively with tuberculous animals.

CASE I.—J. G., aged forty-five years. Was never ill before, and no tuberculosis in his family. His duties were to cut up tubercular and condemned carcasses. In 1892 or 1893 he received a small wound of the middle finger of the left hand, and a nodule soon formed, surrounded by a zone of redness. It increased slowly until 1897 or 1898, when the thermocautery was resorted to with partial success. About a year ago the man tore the first finger of the same hand on a bone from a tubercular cow. The wound cicatrized in about eight days, but later a nodule developed on the site. When examined, in August, 1891, the disease was confined to the first and middle fingers of the left hand. On the first finger nodules about the size of a pea protruded from the surface 1 mm. to 2 mm., moderately red, and having in the center a broken area covered with small crusts. The nodule on the middle finger was much larger and the verrucose condition more developed.

CASE II.—J. O., aged thirty-five years. No history of tuberculosis in family. The patient, his wife, and three children had always been healthy. Has been employed in the abattoir for one year, and always in division reserved for tuberculous animals. Three months before he had suffered a wound of two fingers, following which the disease developed. On the little finger is a hard, rough, thickened area, extending entirely through the skin. On one side is an ulcer which goes deep into the corium.

CASE III.—K. S., aged thirty-eight years. Employed in handling tubercular material. He showed a typical tuberculosis of the skin. As the case was being treated by another physician, the details are not given.

It would seem that instances of infection through wounds are not as uncommon as has been supposed heretofore. Their value has been questioned on the ground that inoculations do not always correspond to natural infections. I do not pretend that such cases settle the whole question definitely, but they do prove beyond question that there is no peculiar quality in the tissues of man which makes him an unfit soil for the bovine tubercle bacillus. Furthermore, they afford us means of comparison with similar cases in which the invading organism is of human origin, wounds of the hand while operating on tuberculous cadavers, or in cleaning cuspidors used by phthisical persons, being not uncommon. I have been at some pains to study the reports of such infections, and feel bound to conclude that the bovine bacillus is at least as virulent as the human for man when introduced in such manner. We know from experimental as well as clinical evidence that the skin is the tissue most unfavorable to the growth of the tubercle bacillus. If, then, the bovine bacillus can successfully invade the skin and multiply there, with the production of characteristic changes, it seems we are fully justified in believing that organs and tissues that are known to offer favorable soil to the human bacillus will also prove favorable to the bovine organisms. On the other hand, I know of no animal which is susceptible to the human bacillus yet immune to the bovine. Birds are equally refractory to both, a small proportion of those inoculated or fed with either succumbing to tuberculosis.

TUBERCULOUS INFECTION THROUGH FOOD. Koch bases his opinion as to the non-transmissibility of bovine tuberculosis to man largely on the alleged rarity of primary intestinal tuberculosis. He says: "If the bacilli of bovine tuberculosis were able to infect human beings many cases of tuberculosis caused by the consumption of aliments containing tubercle bacilli could not but occur among the inhabitants of great cities, especially children." "That a case of tuberculosis has been caused by aliments can be assumed with certainty only when the intestine suffers first—*i. e.*, when a so-called primary tuberculosis of the intestine is found." He says that he has seen only two such cases; that at the Charité Hospital in Berlin only ten cases were seen in five years; that among 933 cases of tuberculosis in children at the Emperor and Empress Frederick's Hospital for Children, Baginsky never found tuberculosis of the intestine without simultaneous disease of the lungs and bronchial glands; that Biedert found only sixteen cases of primary intestinal tuberculosis among 3104 children examined postmortem.

The assumption that the proportion of tuberculosis caused by food is correctly revealed by the lesions of the intestine or mesenteric glands is certainly erroneous, and leaves out of consideration entirely at least one very important avenue of infection.

INFECTION THROUGH THE TONSILS. The numerous observations made of late years leave no doubt that the tonsils sometimes act as the port of entry for the tubercle bacillus. As well put by Baup,[38] "discussion is only possible as to the greater or less frequency of these lesions, and their pathological importance," a position sustained not only by the work of other observers but by his own, in which he examined the tonsils from those cases only in which tuberculosis of the lungs was absent and other ports of entry could be excluded. Dieulafoy,[39] by the inoculation of guinea-pigs, found tuberculosis in fifteen of ninety-six cases. L[illegible],[43] who was careful to employ only the interior portions of the tonsils, in forty-five consecutive cases of children from three months to thirteen years of age, seen at autopsy, found seven which were tuberculous. One of the most recent studies of this subject is that of Friedmann,[40] who examined the tonsils obtained from ninety-one children at autopsy, and fifty-four cases removed by operation, all but one of the latter under five years of age. Of the ninety-one cases, in three there was tuberculosis, probably not primary; in five there was tuberculosis, probably primary, with secondary involvement of lymphatic glands, intestine, and bone; in one the tonsils showed many tubercles, giant cells, and tubercle bacilli, the rest of the body being free; in seven (two with and five without tuberculosis in other parts of the body) the tonsils contained typical giant cells, but no bacilli could be demonstrated; in three giant cells attributed to other causes were found; in eleven, which showed extensive tuberculosis of other parts of the body, the tonsils were free, but showed scars; in four the tonsils were free, there being tuberculosis of the internal organs; in three bacilli were demonstrated in smear preparations, though no tubercles were found. In the remaining fifty-four cases tuberculosis was not found in any part of the body. Only one of the operative cases showed primary tuberculosis.

When we remember the frequency with which children are fed, and the ease with which particles of food lodge in the tonsils, we cannot but think that Friedmann is reasonable in his conclusion that tuberculosis of the tonsils is quite common in children, and that the infection takes place directly from food, and not through the lymph, blood, or by inhalation.

Numerous authors who have studied this question give corroborative facts, lack of time preventing further citations. Those given are sufficient, I think, to show the fallacy of looking exclusively to the intestine for the proof of a food infection. I beg to call attention to the specimen showing ulceration of the tonsils which I have here, taken from one of four pigs which were infected by feeding, ten meals containing pure cultures of tubercle bacilli being given. All the animals contracted general tuberculosis, most marked in the lungs, and ending in death. Three of the four presented lesions of the tonsils similar to those shown, while in only one could any lesion of the intestine be found. In the tonsils of the fourth pig, which showed no macroscopic lesions, many tubercle bacilli and areas of caseation were found. In three of the four pigs the cervical and mediastinal glands were markedly involved, and tubercle bacilli were readily demonstrated in smear preparations made from the cut surface of the salivary glands in the remaining one.

A similar observation was made by Koch, who, however, seems to have entirely overlooked the importance of it. He says: "These animals had without exception severe tuberculous disease, especially tuberculous infiltration of the greatly enlarged glands of the neck and of the mesenteric glands, and also extensive tuberculosis of the lungs and spleen."

CLINICAL OBSERVATION. The number of cases in which infection can be traced to the consumption of tuberculous milk is not large, and almost all of them are open to some criticism from the fact that all other sources of infection cannot be positively excluded. From the nature of the case this will always be true, and we can never shut children up and feed them with tuberculous milk in the way of an experiment. However, evidence in some of the cases is so clear that Nocard has well said: "It has almost the value of an experiment," and it is quite sure that we would unquestionably accept evidence of much less value if any other disease than tuberculosis were concerned.

The cases reported by Stang,[41] Demme,[41] Gosse,[41] Ollivier,[42] and Law,[44] involving nineteen persons, are too well known to need repetition here.

Ebers[45] reports six cases, collected by several observers, of tuberculosis in children, attributed to the milk of tuberculous cows.

Bang,[46] through inquiries in Denmark, has collected reports of nine persons in whom infection could be traced with reasonable certainty to milk from tuberculous cows.

Von Ruck[47] reports the case of a father and child which are very convincing, and says that he has observed several others in which there was very good reason to believe that milk was the agent of transmission for the tubercle bacillus.

Klebs and Rievel[48] have recently reported two cases which came under the observation of the former. A healthy young man employed by Klebs to assist in making some investigations on milk infection had the habit of drinking the milk of the tuberculous cows used in the experiment. In a few months he died of miliary tuberculosis. The second case was one of six male children, who died at the age of two years of tuberculosis of the cord and meninges. This child was the only one of the six fed on cow's milk and the only one that developed tuberculosis.

POSTMORTEM EVIDENCE. The reports of pathologists based on autopsies prove conclusively that in a certain proportion of persons dying of tuberculosis, and especially in children, the infection takes place through the intestine. As to the frequency of infection by this route there is a wide divergence of opinion, due partly, no doubt, to the fact that this method of infection is much more common in some localities than others, owing to local conditions, and partly to the interpretation given to the postmortem findings. Our method of determining the portal of entry is not entirely satisfactory, as is shown by the large number of cases reported by many pathologists in which it is impossible to locate the primary lesion.

In general the determination of the primary lesion is based on the belief that the lymphatic glands in children give evidence of the duration and extent of tuberculous diseases in the organs with which they are in relation. Consequently if the bronchial glands show more advanced caseation than the mesenteric the infection is put down as being through the respiratory tract. The fallacy of this has, I think, been demonstrated as regards infection through the tonsils, and that it is correct, even when the absorption takes place through the intestinal mucosa is open to question. During intestinal digestion there is a constant current from the intestine to the mesenteric glands, and thence up the thoracic duct into the venous circulation. Any tubercle bacilli which may have gained entrance into the stream are carried almost immediately into the lung, and deposited there by election.

It has been shown by Dobroklonski,[49] working under Cornil, that the tubercle bacillus can penetrate the wall of the intestine in the absence of any demonstrable lesion, and that the contact does not need to be prolonged. As the result of carefully conducted experiments on animals he says: "Tuberculosis can certainly invade the body through the digestive tract. For this invasion to occur it is not necessary that there should be either a lesion of the intestinal wall, a desquamation of the epithelium, or any local modification whatever, or an anterior inflammatory process. The tuberculous virus (bacilli as well as spores) can easily pass through the epithelial lining of the intestine when it is entirely normal. This penetration is particularly easy at those points where the contact of the virus with the intestinal wall is prolonged, but it is not necessary that there should be prolonged contact or that it should be any longer than what occurs normally."

In our work at the laboratory of the State Live-stock Sanitary Board we have often been struck by the extensive involvement of the lungs in animals infected by feeding, and the slight injury of the intestines. Indeed, in some animals it has been impossible to detect any involvement of the intestines at all.

I ask your attention to specimens from two animals illustrating these points. The first is from a cow (No. 26435) which was fed with bovine tuberculous material. Both lungs were involved and had cavities in them. The bronchial glands were enlarged, and showed small nodules. The mediastinal glands were enlarged and softened, but showed no nodules. The mesenteric glands were normal, and no lesion of the intestinal wall could be found.

The second is from a monkey fed with a pure culture obtained from the mesenteric gland of a child (Culture BB). Both lungs are involved throughout and to a much greater extent than the abdominal organs. The bronchial glands are enlarged and caseous. In the intestine only one point of injury can be found, and most of the mesenteric glands are normal in size, and show a few nodules 1 mm. in diameter. The glands associated with the upper intestine are much enlarged and show caseation, though not more advanced than what is seen in the bronchial glands.

The specimens from the monkey illustrate another important point, namely, the occurrence of coincident infection through the upper part of the digestive tract and the intestine. If this animal had been examined without the knowledge of its history it would almost certainly have been put down as one of those cases in which the avenue of infection could not be positively determined. The lungs show much more extensive disease than any of the abdominal organs, and the bronchial glands show caseation as well as some of the mesenteric, and to an equal degree. This monkey was tested with tuberculin before the experiment began, and was in perfect health when the feeding with tubercle bacilli commenced. The key to the situation lies in the enlargement and caseation of the cervical lymphatic glands, indicating an infection through the tonsils or some neighboring part of the upper digestive tract, though no lesion could be detected. We have here an undoubted food tuberculosis, yet the respiratory tract shows the chief involvement. Does not the same thing occur also in children, and more often than we suspect?

With these facts in view it seems not impossible that an infection gaining entrance through the intestines may appear first in the lung, and thus be erroneously attributed to the respiratory tract.

On one point all pathologists as well as clinicians seem to agree, that in children tuberculosis shows a marked tendency to become generalized, and this occurs with such rapidity that it is often impossible to decide where the infection gained entrance.

The postmortem statistics are gathered mainly from hospitals and asylums for children, and it is in children that we have most reason to fear infection by food, their diet consisting as it does so largely of cow's milk. The tremendous mortality of children from tuberculosis has forced us to pay particular attention to the study of the factors at work in early life, and a number of interesting and valuable analyses of autopsy records have been published. From England we get the most positive evidence of infection through the intestine, and the most striking proofs of its frequency. English pathologists are practically unanimous in regarding the intestine as a frequent path of infection, the primary lesion being associated with this tract in about 25 per cent. of all cases. We may examine the figures given by some of the more recent writers on this point.

Carr,[50] examined 120 cases at the Victoria Hospital for Children, London. Of these in eighty-two the disease was generalized, in the sense that the lesions in different localities seemed to have a "common simultaneous origin from some infective centre, or else that there were several quite independent tuberculous centers in different parts of the body." In seventy-nine cases the primary lesion was in the lung or bronchial glands; in twenty cases in the intestine or mesenteric glands; in six cases it was impossible to tell whether the respiratory or the digestive tract was first involved; in eleven cases widely separated caseous foci were found, and the primary lesion could not be located; in four cases no centers could be found, the lesions being generalized.

Guthrie,[51] at the Children's Hospital, Paddington, London, examined seventy-seven cases. He considered that in forty-two cases, or 54.5 per cent., the primary lesion was in the respiratory tract; in nineteen cases, or 24.6 per cent., it was in the intestinal tract. Of the remaining sixteen cases the thoracic and abdominal organs were equally affected in seven; in six the original was unknown, and in three otherwise accounted for. In only thirty-two cases could the origin of the tuberculosis be traced with certainty to the glands, to the thoracic seventeen times, and the mesenteric fifteen times.

Still,[52] at the Great Ormond Street Hospital for Children, in 769 consecutive autopsies on children under twelve years of age, found 269 cases which showed tuberculous lesions. Of these 117, or 43.5 per cent., were children under two years of age; and 56.5 per cent.—more than half the total number—were children under three years of age. The origin of the disease was as follows:

Lung	105	138=51.3 per ct.
Probably lung	33	
Intestine	53	63=23.4 per ct.
Probably intestine.	10	
Ear	9	15= 5.5 per ct.
Probably ear	6	
Bones and joints	5	53=19.8 per ct.
Fauces	2	
Uncertain	46	

In forty-three cases in which death was due to other causes, such as diphtheria, heart disease, etc., the primary focus of infection could be determined with great certainty, as the tuberculosis had not become generalized. Among these the primary lesion was respiratory in twenty-six cases, or 60.4 per cent.; intestinal in sixteen, or 37.8 per cent.: and in the ear three times.

Dr. Shennan,[53] of the Royal Hospital for Sick Children, in Edinburgh, found among 278 cases of tuberculosis 28.1 per cent. in which infection had taken place by the intestinal tract, showing that the high percentage in which this route of infection is observed is not confined to London, where it might be supposed that conditions were such as to favor it specially.

The few reports we have from America indicate that infection through the intestine is much less frequent than in England.

Northrup[54] reports that among 125 autopsies in only three was the primary lesion found in the intestinal tract. In thirty-four cases, however, the disease was so general and far advanced that he was unable to determine the mode of invasion.

Holt[55] among 119 tuberculous children examined postmortem found the intestines affected forty times and mesenteric glands thirty-eight times, but in no case did he consider the intestine as the route of invasion.

Bovaird,[56] in 1899, published the records of seventy-five autopsies on tuberculous children. In sixty cases infection had taken place through the respiratory tract; in eight the bronchial and mesenteric glands were equally involved, and in seven the records were incomplete. He has recently[57] added the record of fifty cases, among which two cases of primary intestinal infection occurred. The number of indeterminate cases is not given.

German statistics, as far as I have been able to obtain them, do not sustain Koch's position, although they indicate that primary intestinal tuberculosis is not so common in that country as in England, which we would hardly expect, considering the precautions prescribed in Germany and the lack of regulations in England.

However, intestinal involvement in children appears to be quite frequent in most parts of Germany; and as many of the reports do not clearly indicate the primary seat of invasion, we are justified in believing that a fair proportion of these cases are due to intestinal infection. For example, the statement given by Koch and attributed to Baginsky—that among 933 cases of tuberculosis in children he never found tuberculosis of the intestine without simultaneous disease of the lungs and bronchial glands—is entirely indefinite as to the primary seat of the disease, and as quoted furnishes no ground whatever for Koch to stand on.

Against the figures given by Koch—which are confined to his own experience—the reports of Baginsky, and a series of cases attributed to Biedert, we have the statement of Professor Hueppe[22] that "the number of these cases (primary intestinal tuberculosis) occurring in children is by no means so small as Koch alleged. The number of cases may be fairly reckoned as between 25 and 35 per cent. of all deaths of children from tuberculosis."

Among fourteen children who died from other diseases, and in whom the existence of tuberculosis was not recognized before death, Kossel[58] found tuberculosis of the bronchial glands ten times and of the mesenteric glands four times. In twenty-two children who died of tuberculosis he found the disease confined to the intestinal tract in only one case.

It is unnecessary to quote further statistics on this point. The extent of intestinal tuberculosis varies in different countries and in different parts of the same country—a fact which of itself indicates a local factor, such as the greater or less prevalence of tuberculosis in cattle. One cannot study such statistics as those given without being fully convinced that a very important proportion of the children who die of tuberculosis are infected through their food, and that the report made to the council of the British Medical Association was justified, namely, that "the mortality from tuberculosis in early childhood is not decreasing as it is at other ages in the United Kingdom; and the opinion that this great prevalence of the disease in childhood is due to infection through the alimentary canal by milk from tuberculous cows appears to be well founded."[59]

Extent of Tuberculosis in Cattle. It is well known and so universally acknowledged that tuberculosis is a wide-spread scourge in cattle that it would be superfluous to give an array of figures showing the extent of its ravages in various countries. Those interested in this phase of the subject will find the latest statistics given by Dr. Leonard Pearson in Bulletin No. 75, issued by the Commonwealth of Pennsylvania, Department of Agriculture. In studying such statistics it must be borne in mind that it is in the milch cow, and especially the cow on the dairy farms near large cities, that is most apt to fall a victim to tuberculosis. In Pennsylvania, Dr. Pearson[60] has found that of the tubercular herds tested about 13 per cent. of the animals had tuberculosis. Some herds show a very high proportion of diseased animals. Thus, for example:

Among 174 cattle	166 were tubercular.
73 "	59 " "
22 "	17 " "
14 "	14 " "
20 "	20 " "
59 "	53 " "

In other parts of the State tuberculosis is very rare or even unknown. These places are found in the interior counties, where the stock is "native" for the most part, or were stocked at a time when bovine tuberculosis was very little known in the United States.

There has been and is considerable discussion as to the stage of the disease at which a tuberculous cow becomes dangerous through the passage of tubercle bacilli into her milk. Some authorities hold that there must be actual disease of the udder for this to occur, while others believe that this is not necessary. As early as 1893 Dr. Theobald Smith showed that the tubercle bacillus may be found in the milk of tuberculous cows when the udder, so far as the naked eye could tell, was free from disease. In a series of experiments at the laboratory of the State Live-stock Sanitary Board of Pennsylvania the mixed milk of five cows was examined by intraperitoneal inoculation of guinea-pigs. These cows had reacted to tuberculin, but were in good condition and of fine appearance. Repeated examinations of the udders by several veterinarians failed to reveal any lesion, and examination after the death of the animals gave the same negative results. No attempt was made to concentrate the bacilli; on the contrary, the whole quantity of milk was well shaken, in order to imitate as nearly as possible natural conditions, and moderate doses of milk (10 c.c.) were used. Of eighty-eight guinea-pigs employed in this test sixty-three lived long enough for the development of tuberculosis, and of these ten, or 15.8 per cent., became tubercular.

More surprising and more unusual are the results of Rabinowitsch and Kempner,[61] who inoculated the milk of fifteen cows into guinea-pigs, the experiment being made to determine whether or not the milk of cows having a tuberculosis which could be detected only by tuberculin, and not by physical examination, might be virulent. Three examinations were made by a veterinarian in the course of the experiment. Of the fifteen animals ten were found to give virulent milk, a percentage of 66.6. One cow gave milk which contained a yellowish, gelatinous material, and caused a fatal peritonitis in all animals inoculated. Leaving this out, the positive results amount to 71.4 per cent. All of the cows had reacted to tuberculin, but none showed clinical evidence of udder disease when the experiment began. Of the ten giving virulent milk three showed advanced general tuberculosis, but no disease of the udder; two showed no evidence of disease at all, and one only on the second and third examinations. One cow had rales at the time of first examination, but these disappeared, and she showed no evidence of disease after. On postmortem one cow was found to have tuberculosis of the udder, and one showed clinical evidence of it on the third examination, made six months after the experiment was begun. The authors conclude: "Milk may contain tubercle bacilli, first, in beginning tuberculosis, without discoverable disease of the udder, and, second, in latent tuberculosis that can be detected only by the tuberculin reaction;" also, "milk from cows that react to tuberculin must be suspected of being infectious in every case."

With these results before us we must admit that while tuberculosis of the udder is the most dangerous condition, we cannot by any means regard the milk of cows with general tuberculosis, but the udders of which are free from the disease, as being safe for food. We must insist that danger is not limited to those herds which harbor one or more cows with udder tuberculosis. I cannot agree with those writers who attempt to belittle the dangers to which milk-fed babies are exposed by pointing out the comparative infrequency of tuberculosis of the udder. Dilution with the milk of other cows free from tuberculosis no doubt lessens the danger, but does not remove it.

Acid-fast Bacilli. A few years ago Möller announced the discovery of a bacillus having the morphology and staining reactions of the tubercle bacillus. He has shown that this bacillus and others closely allied to it may constantly be found in forage and in the feces of animals fed on such forage. Petri, Rabinowitsch, Grassberger, Korn, and others have found the same or like bacilli in milk, butter, and margarine; Rabinowitsch has isolated one of the same group from a case of gangrene of the lung in man; Karlinsky has shown their presence in nasal mucus, and Marpman has found them in urine, so that we know that this group of "acid-fast" bacilli has a wide distribution in nature. The property of resisting decolorization by mineral acids was for a long time considered diagnostic of the tubercle bacillus. The discovery, therefore, of a comparatively large group of organisms having the same property, and being indistinguishable morphologically under the microscope, has served to throw some doubt on researches in which the microscope has been relied on entirely to demonstrate the presence of the tubercle bacillus in milk. Animals such as guinea-pigs and rabbits inoculated intraperitoneally with cultures of these bacilli, or with milk, butter, etc., containing them, develop nodules which may sometimes be mistaken for tuberculosis. However, such mistakes must be rare, and there can be no doubt that the true tubercle bacillus passes into the milk of tubercular cows, as shown above. Reinoculation, microscopic examination of the tissues, and the isolation of cultures can be relied upon to clear up the diagnosis of any doubtful cases.

SOLUTION OF THE PROBLEM. In the solution of the problem before us the most directly valuable data will, I think, be obtained from the examination of cultures isolated from the abdominal organs of children in whom there is reasonable evidence of infection by the intestinal tract. When these cultures are found to have a high degree of pathogenic power, and are able to infect cattle in moderate doses, we will be justified in saying that the children from whom they were obtained were infected in the first instance from bovine sources. By the examination of a large number of such cases we will, I believe, obtain very valuable information as to the frequency with which children are infected by milk. On the other hand I do not consider that we can entirely exclude bovine infection even in those cases where the abdominal organs yield a culture of feeble virulence, for the reason that we at present know nothing of the effect produced on the bovine bacillus by prolonged residence in the human body. It is certain that the various types of tubercle bacillus known to us have sprung from a stock common to them all, and that they have acquired their racial peculiarities by residence in different animals, through which they are subjected to a difference in food, temperature, and resistance. In other words, the struggle for life is carried on in the various species of animals under varying conditions, the result being that in each animal the tubercle bacillus acquires properties which best enable it to carry on life in that particular host. The acquisition of these peculiarities no doubt requires a certain lapse of time, but how much we do not know. We have experimental evidence that it does not require a great time to change the tubercle bacillus from a higher into a lower type. By the method of inoculation in the peritoneal cavity in collodion sacs Nocard[62] has shown that in from five to eight months both the bovine and human bacillus can be made to acquire the cultural characteristics of the avian bacillus, and to a certain extent its pathogenic action also. A few passages from fowl to fowl during four to six months increased this greatly. By passage through the blind worm Möller[63] has in the course of a year so changed the human tubercle bacillus that it grows like the organism of fish tuberculosis, and has the same temperature reactions. It grows best at 20° C., and ceases to grow entirely at 30° C. The bacillus of fish tuberculosis, discovered by Dubard,[29] had for its origin the human bacillus, the fish having fed on the sputum and dejecta from a patient far advanced in phthisis. The fish had been subjected to this for about a year before the disease was noticed.

With these facts before us I do not think we are forcing a point in believing that it is at least possible for the bovine bacillus to become rapidly so changed in the body of man that it will show the cultural and pathogenic peculiarities which we find usually in cultures of human origin. For these reasons our observations should be made by preference on cases which are rapid and acute.

CONCLUSION. The evidence at hand forces us to conclude that human and bovine tuberculosis are but slightly different manifestations of one and the same disease, and that they are intercommunicable. Bovine tuberculosis is, therefore, a menace to human health. We are not in a position at present to define positively the extent of this danger, but that it really exists cannot be denied. In the past there has probably been a tendency to exaggeration, but however great this may have been it does not now justify any attempt at belittling the risk, and it is folly to blind ourselves to it.

The eradication of bovine tuberculosis is amply justifiable from a purely economical stand-point; viewed in its bearing on human health it becomes a public duty.

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April 24, 1902.

Uterus, Gross Specimen and Sections; Also Sections of the Liver, Kidney, and Bladder from a Case of Puerperal Sepsis Due to Mixed Infection by the Cocci of Suppuration and the Bacillus Coli Communis and Other Organisms; Also a Preliminary Consideration of a Morbid Process Affecting Unstriped Muscle (Particularly the Elastica), and Not Heretofore Described.

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Abstract of Clinical History.[1] Mrs. O., aged thirty-nine years, American; admitted to Jefferson Maternity third day of labor, after repeated unsuccessful attempts at forceps delivery. Condition on admission: Temperature, 97°; pulse, 150; respiration, 26; shock, slight delirium; uterus in state of tonic contraction; bladder greatly distended; albuminuria, with finely granular and hyaline casts; urea, 1.1 per cent.; bacteria numerous; vertex presenting; highly contracted justominor pelvis; usual treatment of shock. As thorough asepsis as possible; catheterization, craniotomy, delivery, fetus macerated. Uterine cavity cureted and packed with iodoform gauze. Transfusion, hypodermoclysis (repeated), stimulation, one intrauterine douche. Exhaustion, death second day after delivery.

Autopsy held ten hours after death. Permission to examine the abdominal organs only. Anatomic diagnosis: Hemorrhagic and suppurative peritonitis, acute splenitis, diffuse nephritis, renal infarction (anemic), pyelitis, ureteritis, cystitis (partly hemorrhagic), septic metritis (puerperal), lacerations in vagina and perineum, acute gastric dilatation, focal necroses in liver. Cause: Infection. Organisms found: Staphylococcus pyogenes aureus, Bacillus coli communis, Diplococcus pneumoniæ, Bacillus diphtheriæ (?).

Body of a well-nourished female. Marked rigor mortis. Extensive suggillation over posterior part of trunk. Over the anterior abdominal wall and extending laterally are numerous subcutaneous hemorrhages; some are petechiæ, others more diffuse; none is over 0.5 cm., and majority scarcely more than 2 mm. in diameter. Just below the right iliac crest is an old fibrous cicatrix 6 mm. in length, 4 mm. in width, its long axis approximately parallel to iliac crest. Skin of abdomen shows usual signs incident to pregnancy; pigmentation in median line conspicuous.

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[1] For the privilege of using the clinical history in this case I am indebted to Professor E. P. Davis.

Subcutaneous fat normal in quantity and texture. The extraperitoneal fat is edematous.

On opening the peritoneal cavity there is found a small quantity of a brownish-white, flaky fluid (not sufficient to measure). This fluid posterior to the uterus yields an offensive odor. When the organ is raised and the pelvic cavity exposed it is found to contain a fibrinopurulent exudate which surrounds the rectum, occupying Douglas' cul-de-sac and supplying a filmy, grayish-yellow coat over the adjacent structures. The parietal peritoneum is beset with numerous hemorrhages (petechial and diffuse), and is markedly hyperemic; similar areas of rhexis are present over the intestinal coils, but are not abundant.

The spleen is attached by an old capsulitis to the diaphragm, the pulp is rather pale, the Malpighian bodies grayish, and the organ a little softer than normal.

The left adrenal is unusually large and measures 2.5 cm. in length, 2 cm. in width, 1 cm. in thickness, shows areas of hemorrhage, and is somewhat edematous; weight, 10 gms.

The left kidney is small, resists incision; the cortex is swollen and markedly striated, the capsule strips smoothly, subcapsular vessels are conspicuous, labyrinth and tufts are decidedly hyperemic, the intervening areas pale and yellow. The pelvis and ureter are slightly dilated, moderately distended, and on section a mucopurulent fluid escapes.

The right adrenal is a small club-shaped organ 4 cm. long, 1.5 cm. wide, 0.5 cm. in thickness; it presents nothing noteworthy.

The right kidney cortex shows changes similar to those described as present in the left; the pelvis and ureter are distended; the former but slightly, if at all, dilated; contents same as on left side. The ureter presents an irregular sausage-like dilatation, extending to the bladder; its size when distended is about that of a large thumb.

About the middle of the kidney is an irregular, pale-white area, involving most of the medullary portion. It is fan-shaped, the apex corresponding to the apex of the pyramid and radiating toward the cortex, which is partly involved. This is evidently an area of coagulation necrosis possessing the gross characters of an irregular anemic infarct. (Note.—As it was desired to preserve this organ as a gross specimen, the area was not removed for histologic study.)

The bladder is moderately distended, reaching 6 cm. above the pubes; its wall is thick, and the veins over the lower part of the organ distended and thrombosed. The mucosa of the bladder is irregularly mottled with purplish spots, which appear to be diffuse areas of hemorrhage situated in the submucosa. The contained urine is opaque, contains flocculi, and is slightly offensive.

The uterus extends to the umbilicus, is slightly pyriform; weight, 700 gms. Organ is flattened in its anteroposterior diameter. Just within the cervix posteriorly is a slough that marks the site of what appears to have been a laceration, 2 cm. in length and 1 cm. in depth, its long axis corresponding to the axis of the organ. It does not extend through the uterine wall, but the underlying structures are soft, grayish-black in color—in other words, necrotic, the necrosis extending to the peritoneal surface posteriorly. There is no solution in the continuity of the peritoneum. The organ is incised on its anterior aspect; the wall at its thickest point, just above the middle, measures 3.75 cm. Fundus measures 1.75 cm. in thickness.

The interior of the uterus is lined by a grayish-brown, soft, shreddy, necrotic mass of tissue spread quite uniformly over the entire surface of the organ. At points the grayish necrosis extends into the uterine wall to a depth of 0.5 cm.; it gives off an extremely offensive odor. Just external to this layer is a grayish zone varying in width; at the fundus it approaches 1 cm. in thickness, while toward the cervix it scarcely exceeds 4 or 5 mm. It is not uniform in breadth, and its outer margin is limited by an irregular reddish line from 1 mm. to 2 mm. in breadth. The grayish zone is evidently the area of extending necrosis, and the reddish line the limiting area of leukocytic infiltration and vascular dilatation. External to the reddish line the muscle shows no conspicuous gross change.

The peritoneal coat is roughened, red, and injected; over the posterior and inferior surfaces there is a slight, scarcely perceptible, fibrinous deposit that becomes more evident as the lower margins are approached. The ovaries are hyperemic. The Fallopian tubes seem slightly swollen; on opening them the mucosa is found to be reddened, but free from evidence of necrosis or suppuration.

The vaginal mucosa is turgid, at points purplish. Along the right wall, extending from the vault downward, is an irregular, ragged slit, with blackish, necrotic sides and floor. It is not possible to determine with certainty that this was a laceration, as it seems probable that a similar condition might have resulted from infection and necrosis; it measures 5 cm. in length. At a number of points the mucous membrane is eroded and necrotic. With the exception noted above, the necroses are superficial.

The vulva: The labia are edematous, although not markedly so. The urethral orifice is red and pouting. There is a slight laceration in the perineum. The external genitals and lower part of vagina are in better condition than internal genitalia.

The surface of the liver is beset with whitish areas, presumably areas of necrosis; on incision similar grayish or yellowish-white areas are disclosed; they are for the most part barely perceptible, rarely attaining a diameter of 2 or 3 mm. The remainder of the surface shows the usual cloudy swelling. Gall-bladder moderately distended by dark viscid bile; ducts patulous.

The stomach is enormously distended, extending down to umbilicus. The duodenum is flaccid. Capacity of stomach estimated at 5000 c.c. It could not be demonstrated that the gastric dilatation was in any way due to kinking on superior mesenteric vessels and nerve. The interior of the intra-abdominal alimentary canal manifests no conspicuous abnormality.

The pancreas showed no gross lesion.

Inoculations were made from renal vein, spleen, ureter, and interior of uterus.

Morbid Histology. Specimens from the spleen, kidney, liver, uterus, and bladder were fixed, infiltrated with paraffin, and stained by the usual laboratory methods. The stomach was ordered preserved; but, unfortunately, the instructions were not followed.

Spleen: While this organ contains areas of focal necrosis, they are, on the whole, less conspicuous and less advanced than those in the liver. The pulp is everywhere distended by erythrocytes, rich in leukocytes, and unusually abundant are the large endothelial cells commonly present in many infectious diseases. As usual, these cells show phagocytic activity, many containing fragmented erythrocytes and pulp cells. The pulp contains pigment and fragmented red cells; the Malpighian bodies are not unusually conspicuous. The fibrous tissue forming the trabeculæ is swollen, and the endothelial cells of the sinuses exfoliating and unusually prominent, although karyokinetic figures or other morphologic evidence of active proliferation has not been recognized. The changes seen, as indicated by the foregoing, are those usually found in the spleen subjected to the noxious action of toxic bodies circulating in the blood, and in particular the result of bacterial toxins.

Liver: This organ contains, throughout all the sections examined, multiple necroses. For the most part the areas of necrosis are small, rarely attaining a diameter of 2 mm., and in most instances are purely microscopic, involving but a small part of a single lobule. They are usually quite regular, although not constantly so, and are distributed in various areas of the organ, not always involving any part of the lobule, some being situated at the periphery and others more centrally. The hepatic cells are no longer to be recognized in the centers of the areas of necrosis. Usually toward the periphery can be seen, however, a hazy outline of cells, the protoplasm of which is so far disintegrated that it no longer elects even such strongly acid dyes as eosin. The margin of the necrotic area is usually fairly defined, but often it can be observed that the change merges with the surrounding hepatic structure. A few polymorphonuclear leukocytes can be recognized in the areas of necrosis and an occasional hyaline cell. There are masses of fragmented chromatin, evidently relics of the nuclear contents of hepatic cells. Evidences of regeneration are entirely wanting, and only a few cellular elements of the kind usually grouped among the scavenger cells that are supposed to be influential in removing this dead material are to be recognized. These cells are large, round, or ovoidal, of that type described by Chantemesse and Podwyssotsky. The hepatic cells surrounding the areas of necrosis, and, indeed, practically all the liver cells, are advancedly granular, the cell outlines poorly defined, the protoplasm but faintly staining, the nuclei often indistinct, and in some instances fragmented. The capillaries are singularly free from blood; no evidence of rhexis in the perivascular tissues. The biliary channels in most of the sections are difficult to identify by reason of the granular and necrotic changes that have occurred in the canalicular epithelium. The epithelium, when still present, is usually granular, with poorly staining nuclei, and the cells not infrequently detached and lying within the lumina of the ducts. The endothelium of the capsule is swollen, at points detached, hyaline or advancedly necrotic, evidently participating in the associated peritonitis.

Kidneys: The bloodvessels of the capsule are intensely engorged, and at a number of areas immediately beneath the capsule accumulations of lymphoid cells are to be observed. Occasionally there is a small subcapsular extravasation; such areas of rhexis are, however, infrequent and minute. The changes observed in the cortex are for the most part restricted to the areas of the labyrinth. The epithelium of the convoluted tubes is often granular, desquamating, the margins of the epithelial cells no longer defined, the nuclei frequently hazy, poorly staining, and in some instances the entire cell detached from the basement membrane. The lumina of these tubules almost constantly contain a finely granular, strongly acidophilic detritus, probably partly exudative in point of origin, but presumably, for the greater part, formed from fragmented protoplasm derived from disintegrated epithelial cells that have fallen into the tube. The intertubular tissue is often swollen and in some instances occupied by lymphoid and plasma cells, the former predominating. The straight tubules of the cortex have not escaped changes similar to, though less in degree, than those already described as present in the convoluted tubules. The tuft changes are variable; some of the tufts are swollen, quite filling the capsule, others somewhat shrunken. In practically all of them there is a conspicuous excess of nuclei, apparently belonging to cells largely, if not wholly, of the lymphoid type. Some of the tufts have retracted or are compressed by a finely granular, intensely acidophilic material occupying the space between the tuft and external capsule.

The tubules of the medullary pyramids (Malpighian tubes, loops of Henle, etc.) are not profoundly altered; the epithelium does not stain with its wonted intensity, nor is its protoplasmic outline accurately preserved; many of the nuclei are diffusely stained and but dimly outlined. The intertubular connective tissue is hyperemic, the vascular distention being more marked than in the cortical portion, in which the bloodvessels are but moderately filled.

The pelvis of the kidney, the ureter, and the bladder show practically the same alteration; it is most advanced in the last named organ, which alone will be described.

Bladder: At no point in the vesical mucosa is the epithelium normal. For the most part it has exfoliated or is exfoliating, necrotic, staining poorly, its cells granular, often hanging by loosely attached necrotic shreds to the underlying structures. Beneath the epithelial layer the connective tissue matrix is swollen, hyaline, infiltrated by leukocytes, mostly of the polymorphonuclear type, and in a number of areas showing distinct hemorrhages. Sometimes along the entire margin of the submucosa for from 0.1 to 0.5 cm. a diffuse erythrocytic massing can be recognized, although it is impossible to detect lesions in the vessel walls from which the erythrocytes have escaped. In some of the smaller bloodvessels adjacent to the mucosa the endothelium is swollen, and occasionally leukocytic margination can be recognized. Swelling is evident between many of the complexes or fasciculi in the muscle layer of the bladder, but such swollen tissue is usually quite free from leukocytes.

One of the most interesting conditions observed in this organ, and so far as the writer is aware not previously described in discussion of changes resulting from infection, is a type of hyaline or necrotic change clearly of the same kind as has been frequently observed and accurately described as occurring in the myocardium. In areas showing this change the following alteration can be found.

As will be evident later, the appearance of the morbid process observed in the areas where the change is most evident are greatly influenced by the stain used. When the sections have been treated with the usual nuclear dyes—combinations of hematoxylin or carminic acid, thionin, toluidin blue, safranin, Unna's polychrome blue, or alkaline methylene blue, or similar basic dyes preceded or followed as may be appropriate by acid dyes—the results attained may be summarized as follows:

The change does not appear to involve all of a muscle bundle (smooth muscle complex). In one instance less than one-half of a large band, itself less than 2 mm. in diameter on transverse section, is involved. Under very low magnification it is easily seen that the involved portion of the muscle band containing a large number of fasciculi elects acid stains with intensity, while the remaining portion of the band possesses its normal tingibility.

Under a higher magnification (25 mm., obj. No. 1 eye-piece) it is seen that in this particular band the area involved has lost its sharp differentiation from surrounding fasciculi. The usual narrow rather clear space that surrounds the normal complex is now occupied by a quite hyaline acidophilic substance.

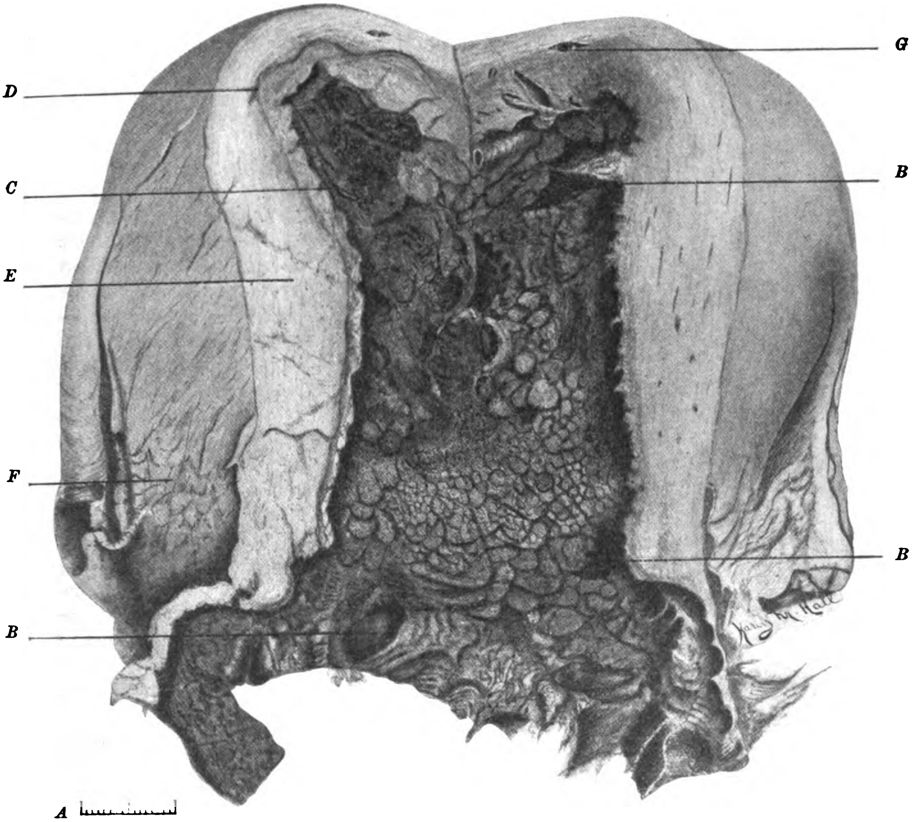
Under still higher magnification it is observed that within the complexes the delicate connective tissue (protoplasmic bridges?) between the individual muscle cells is now replaced by a hyaline homogeneous acidophilic structure that quite obscures the individual fibers. The condition of the cells in the area involved varies at different points, and even adjacent cells show slightly different changes. The interpretation of the changes within the cells is rendered somewhat difficult by the fact that on transverse section no two cells are divided in exactly the same plane, and hence juxtaposed elements might manifest precisely the same changes, but appear different by reason of the position in the cell through which the section passes. I have not been able to secure a fully longitudinal section of a fasciculus showing the alteration in question, although some longitudinal bundles present evidences of the change. The transversely incised cells, the incision involving what, by position and study of serial sections, appears to be the nuclear area, usually show no nucleus, or when present the nucleus stains but faintly or not at all; it is sometimes distinctly fragmented and often irregular and not presenting its normal sharply rounded outline. Occasionally immediately around the nuclear area is a clear space outside of which may be seen a narrow band or simply the illy defined periphery of the cell. In other instances the protoplasm will be found swollen, finely granular, intensely acidophilic and without evidence of vacuolization. In some cells the nucleus is eccentrically placed; there is a distinct vacuole occupying the major portion of the transversely incised cell. The sharp outlines of the normal muscle cell are frequently lost in the hazy periphery that merges into the hyaline substance to which reference has already been made. Under magnification of 1000 diameters this hyaline substance presents at points granules, and occasionally a resemblance to fibrils. It is usually free from nuclei and cells. It is perfectly clear in some areas that it has resulted in part at least from disintegration of the protoplasmic tips and bridges of the muscle cell.

The most interesting disclosure of this extraordinary change is that afforded by sections stained first by Weigert's elastic stain followed by some suitable nuclear and contrast stain. Hematoxylin followed by eosin, or, better, Van Gieson's mixture, yields satisfactory results; but by far the most brilliant findings are observed in sections stained with carmalum, followed by picric acid. In sections stained for elastica it is found that nearly all that structure designated hyalin in the description of mounts stained by ordinary methods has now elected the elastic tissue stain and stands out as a most striking feature, enabling one even by the unaided eye to designate the areas in which the most conspicuous alteration can be seen. Under the higher powers of the microscope (2.5 mm., homo. im.) the muscle cells of unaffected areas are found to be surrounded by a distinct limiting band of extreme thinness—a faint filament--that seems to bind adjacent elements together. In such areas the muscle cells show no conspicuous alteration, the nuclei staining about as the normal, possibly with slightly less intensity, but certainly not in a manner that, in the absence of other lesions, would attract attention. In the areas that, by other methods, previously showed in the most striking way the presence of such reactions as are commonly observed in many infections, and usually looked upon as manifestations of hyalin metamorphosis—the body that previously elected the stains sometimes regarded as characteristic of hyalin now elects to a large degree the Weigert stain. The intercellular spaces immediately surrounding the muscle cells are now occupied by the slaty black greatly altered elastica. In the uninvolved muscle complexes the elastica is a most delicate filament, smooth and uniform, lying closely to the adjacent cells; in the altered areas it is coarse, rarely filimentary but rather nodular, looking like irregularly beaded strings that distend the intercellular spaces. It is evident that the elastica is swollen to two or three times its normal volume and that in the progress of this swelling the muscle cells have been greatly altered. From the study, so far progressed, it is not possible to say that all the material that appeared hyalin is now shown to be elastica, but certainly an overwhelming preponderance gives a perfectly characteristic elastica reaction. The irregular nodular or beaded appearance would at first appear to be due to a pure sectional view of elastic fibers, but in the immediately adjacent unchanged muscle the reaction is that of lines surrounding the muscle cells, and only here and there the suggestion that dot-like bodies are really sectional areas of fibers. The possibility that muscle cells are surrounded by an elastic membrane has been considered, but no conclusion is as yet justified by the findings. If such a membrane be present it is reasonable to assume that it must be fenestrated, and hence on section, when greatly swollen, the points of net-like junction would be most conspicuous. The lesion is so located in one of the blocks of tissue examined in this series that it has been possible to serial a complex through over 1 cm. and show that it follows and is largely limited to the complex involved, not extending, in this instance at least, to juxtaposed complexes, although a second complex showing the change was encountered while following out the first observed; the two were not apposed, but both are mesially placed in the muscle layer of the vesical wall.

The ultimate character of the alteration will be discussed in some later communication in which will be recorded the results of study of the change in this form of muscle in a number of conditions and in the heart, for it has been possible to develop conclusive proof that the heart may be similarly affected.

As regards the peritoneal surface of the bladder, the endothelium of the serous layer is for the most part exfoliated. The subserosa is swollen and infiltrated by both cocci and bacilli, and shreddy

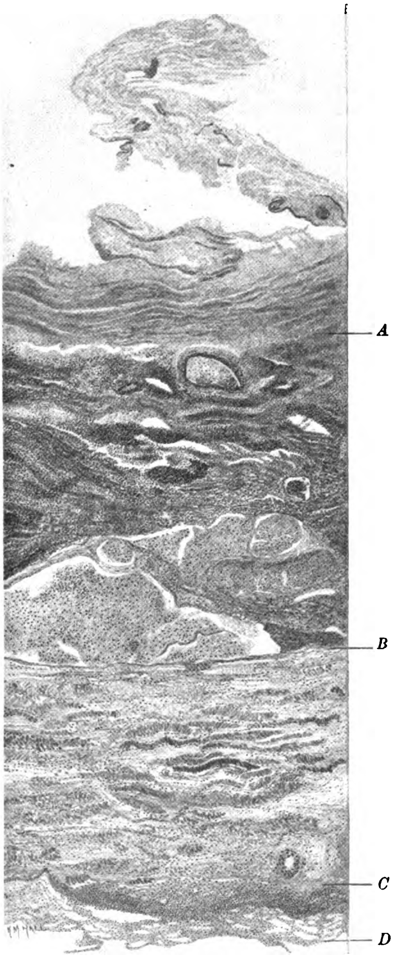
Fig. 1.



Uterus laid open by incision through anterior wall. *A*, Scale, 1 inch. *B B B*, Cavities formed by extensive necrosis. *C*, Necrotic zone, that, on its inner surface, projects as a shaggy layer, fragmenting stratum, and externally is bounded by *D*, the line of hyperemia and leucocytic accumulation (see Fig. 2). *E*, Muscle layer not presenting any conspicuous gross lesion. *F*, Peritoneal surface: early stage of serofibrinous inflammation (the block of tissue from which the microscopic drawing was prepared was taken from just above this point.) *G*, Thrombosed sinus. (Copyright, William M. Warren.)

fragments of necrosing tissue project from the surface; the blood-vessels are intensely engorged and occasionally thrombosed; areas of true rhexis are not abundant. At points in the submucosa other than those mentioned, and in the subserous layer, a few extravascular erythrocytes can be seen, but the sections have failed to catch areas in which the hemorrhage was shown clearly macroscopically. It is probable, however, that the appearance of hemorrhage was exaggerated in the macroscopic specimen by reason of the fact that the masses of necrotic tissue closely resembled

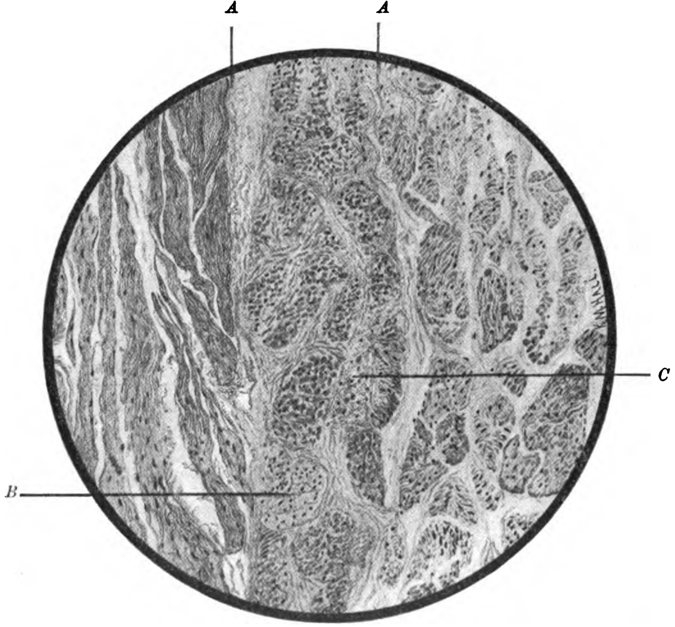
FIG. 2.



Uterus fixed in Zenker's fluid, paraffin, eosin, and toluidin blue. (Obj., Leitz 16 mm. oc. compensation, and reduced two-thirds.) *A*, Above this point is the necrotic layer consisting of granular detritus containing enormous numbers of bacteria (see text), fragmenting histologic elements, and leucocytes. *B*, From *A* to *B* is the zone of hyperemia, leucocytic invasion, and progressing mycotic infiltration. Numerous uterine sinuses are shown, as well as arteries, all occupied by thrombi. *C*, From *B* to *C* muscle showing hyalin (?) change. This part of the section is only a narrow rim of the actual muscle; nothing would have been gained by showing the entire thickness. Just above and to the left of *C* is an artery the endothelium of which is proliferating. *D*, From *C* to *D* is shown the greatly altered serous covering. The layer represented in the drawing is largely composed of fibrin with entangled leukocytes and endothelial cells. (Copyright, William M. Warren.)

distinct areas of hemorrhage. The richness of these structures in bacteria is one of the most conspicuous of the many abnormalities; cocci and bacilli are abundant in nearly all the sections, and so intimately associated that both must have been active simultaneously.

FIG. 3.

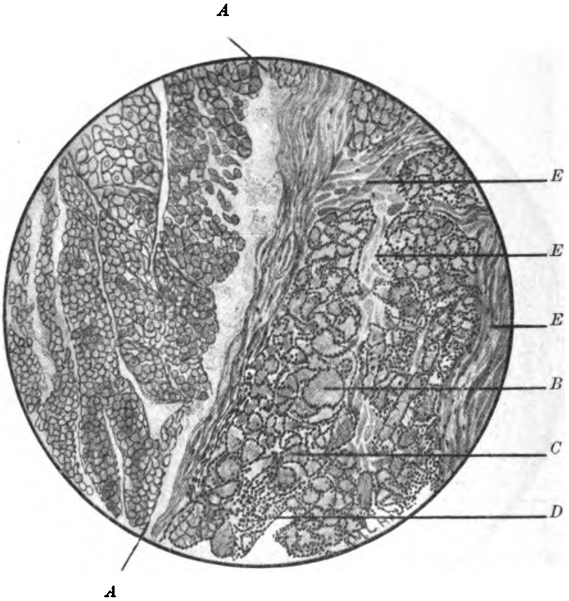


Bladder fixed in Bensley's solution, paraffin infiltration, stained with eosin, followed by thionin. Composite field built up from different areas in the same section. (Obj. Leitz 16 mm., apochromat. compensating oc., reduced nearly one-half.) *A A*, Between these letters is a band extending vertically through the field and showing the most marked hyalin change. *B*, Area with marked intrafascicular hyalin change. *C*, With eosin and thionin this area appears granular, electing the acid dye. Between *C* and *A* is the larger part of a quadrant in which the nuclear fragmentation swelling and necrosis is marked; there is, however, less hyalin. (Copyright, William M. Warren.)

Uterus. Sections from a number of points in the uterus were prepared, but only those will be described that were taken from near the fundus on the anterior surface. In none of the sections so far examined has it been possible to detect the presence of placental tissue.

The conditions found are those of overwhelming infection, as evinced by the abundance of leukocytes, hyalin (?), and necrotic changes in vessels, connective tissue, and muscle, the presence of thrombosed sinuses, etc. The thrombi contain large numbers of bacteria, in some places the bacteria staining with such intensity that the individual elements cannot be made out even in the thinnest sections.

FIG. 4.



Bladder wall fixed in Bensley's solution, paraffin infiltration, stained by Weigert's method for elastica, followed by carmalum and picric acid. (Obj. 2.5 mm., homo. im., compensating oc., and reduced one-fourth.) *A A*, That part of the field lying to the left of leaders from these letters represents the practically unaltered fibers on transverse section. Cells sectioned through the nuclear areas show contained nucleus. The delicate pericellular structure electing the stain for elastica is shown. The area to the right contains a part of the muscle complex manifesting the change described in the text. The beaded elastica is universal; the smooth, delicate fibrils shown in the normal field are absent. *B*, Greatly swollen cell. *C*, Fragmenting cell. *D*, Area from which muscle cells have largely disappeared. *E E E*, Swollen connective tissue that at points is granular. (Copyright, William M. Warren.)

The inner aspect of the organ (uterine cavity) is formed by a hyaline and granular necrotic tissue in which but few cellular elements can be stained; shreds of uterine muscle project into the cavity and are covered and infiltrated by both cocci and bacilli; immediately beneath this necrotic layer is an intensely stained zone containing polymorphonuclear leukocytes, a few hyaline cells, and an abundance of cellular detritus and many bacteria. Sometimes in this zone and sometimes beneath it one recognizes the presence of thrombosed sinuses; the contained thrombi are composed of blood cells, many of which are fragmented, and a small amount of demonstrable fibrin. The margin of these sinuses is formed by walls of leukocytes, many of which are fragmenting, and within the necrosing thrombus innumerable bacteria are variously grouped. In some areas cocci predominate; in others the conspicuous organism is a bacillus possessing the stain reactions and morphology of a member of the colon group. While the thrombosed sinuses are often conspicuous near the inner aspect of the uterine wall, many are more deeply situated. Occasionally smaller vessels and even arteries are thrombosed, and around these one recognizes mantles of polymorphonuclear leukocytes constituting a veritable purulent infiltration of the perivascular tissues. The serous covering of the organ and the superficially placed muscle show practically all the changes already described as present in the bladder. They are possibly less conspicuous, or, it may be, less advanced.

Bacteriologic Report.[1] The specimen consists of agar tubes inoculated from the renal vein, uterus, peritoneum, right ureter, and spleen, and spreads made from the peritoneum.

No growths developed in the tubes from the renal vein and spleen.

The culture from the right ureter contains a bacillus that possesses the morphology and tinctorial reactions of bacilli of the colon group, and a coccus that corresponds to the staphylococcus pyogenes aureus.

From the uterus and peritoneum a pure culture of the same bacillus was obtained.

The spreads contain polymorphonuclear leukocytes, hyaline cells, and what are probably endothelial cells. There is also present an enormous number of bacteria. Some of the bacteria are arranged in irregular zooglea, so that the individual organisms cannot be distinctly made out. Cocci are seen that correspond morphologically to the ordinary cocci of suppuration. Encapsulated cocci possessing the morphology of the diplococcus of pneumonia are also present. This organism was not obtained in the cultures, and hence its identification must remain doubtful. The spreads also contain intracellular diplococci resembling slightly the gonococcus, but they retain the dye by Gram's method.

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[1] I am indebted to Dr. Randle C. Rosenberger, bacteriologist to the Jefferson Medical College Hospital, for bacteriologic examination and report here incorporated.

Bacilli are also seen, some 2μ to 5μ in length, 0.3μ to 0.4μ in thickness; others 4μ to 5μ in length, with ends slightly clubbed. The bacilli first mentioned occurred in pairs, ungrouped, and in short filaments, and decolorize by Gram's method. The larger bacilli occur principally ungrouped, possess granules reacting to Neisser's stain, and retain the dye when treated by Gram's method. They resemble the Bacillus diphtheriæ morphologically and tinctorially, but were absent from the cultures.

The lesion is undoubtedly one of mixed infection, the conspicuous organisms in the process being (1) the ordinary pyogenic staphylococci; (2) the Bacillus coli communis, or an allied member of the colon group; (3) bacilli that morphologically and tinctorially esemble the diphtheria bacillus (the last named were few in number and were not obtained in culture); (4) Diplococcus pneumoniæ.

The organisms found were distributed as follows: in spreads, pyogenic staphylococci, Diplococcus pneumoniæ, Bacillus coli communis, Bacillus diphtheriæ (?).

From the uterus and peritoneum pure cultures of a bacillus of the colon type, although films and sections show that in both situations other organisms were present. In culture from the right ureter a bacillus of the colon group and staphylococcus pyogenes aureus.

Remarks. The examination of the viscera in this case was restricted to those mentioned, and the report is, therefore, lacking in fulness. The findings in the tissues examined are those expected in a septic process, and have been given in detail as completing so far as possible the anatomic picture with which the unique changes in the bladder, uterus, and ureteral wall were associated. The detailed study of the structural and microchemic alterations in the bladder wall seems to open a wide field for speculation and investigation. Changes in the muscle of stomach and intestine of the kind here recorded would elucidate many complex clinicopathologic phenomena at present not fully appreciated—*e. g.*, acute dilatation of the viscera named in many conditions, sepsis, peritonitis, inflammations of the mucosæ, typhoid fever, etc. The demonstration that in this case what appeared on first examination to be a form of hyaline degeneration of a type identical with that described in the heart, vessels, etc., was later found to be the result of some change in the elastica, intercellular bridges, etc., suggests the possibility that what has been looked upon as a type of hyaline necrosis when seen in other organs or tissues, on further examination may prove to be the result of alterations in the elastica, primary or secondary to alterations in the muscle cells.

The condition observed in this case resembles closely, if it be not identical with, the described necroses that occur in the heart in various infectious diseases, and should further observation establish that in infections the unstriped muscle fibers of the body are liable to necrotic, coagulative, or other retrograde changes, such as are well known to occur in the heart, we would have a satisfactory explanation of the dilatation of the stomach and intestine, yielding of the arterioles, overdistention of the capillaries, the occurrence of hemorrhage, and many other admittedly confusing problems. The comparatively recent introduction of an acceptable stain for elastica places us in a position to examine anew all those conditions upon which it promises to throw a flood of light. While the observations here recorded do not seem to justify any conclusions as to whether the change is initial in the elastica, with secondary wasting and disappearance of the cell, or the reverse, it may be possible by a more extended study of the subject to formulate a definite opinion as to this very important question. The two changes appear so intimately associated in the specimens examined that it seems quite impossible to separate them, and, though studied by every method at my command, it has not seemed possible to give either precedence; sometimes the pericellular elastica may be swollen slightly without conspicuous change in the cell-body or nucleus; on the other hand, the last named structures may be altered without evident abnormality in the elastica, but the overwhelming evidence is that the two changes occur together.

Multiple Infection by the Bothriocephalus Latus: Specimen of Two Entire Worms.

ROBERT N. WILLSON, M.D.

The case presented is that of a Russian Jewess, aged forty-six years, who fifteen years ago noted segments of tapeworm in the stools. She has since passed strings of segments at varying intervals, and brought with her when first seen by me (1899) a small pailful of the same for inspection. Over eighty-two feet of segments were obtained at this time, all of the Bothriocephalus latus, and undoubtedly representing two or more parasites. Two ribbons of segments projected from the anus of the patient for over twenty-four hours, both decreasing in size as the bowel was approached. The specimens exhibited demonstrate the presence of two parasites at least, two heads being included in the mass, and the segments indicate that probably a third parasite was in the bowel, though a corresponding head is missing. The blood count was: hemoglobin, 60 per cent.; erythrocytes, 5,120,000; leukocytes, 16,000. There were no indications of the bothriocephalus anemia, although there was a considerable number of normoblasts present and a moderate eosinophilia.

March 13, 1902.

Proceedings

of the

Pathological Society of Philadelphia.

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A Case of Hypernephroma of the Kidney following Pregnancy.

GEORGE M. BOYD, M.D.,
AND
JOSEPH MCFARLAND, M.D.

The following case of tumor of the kidney appears to deserve mention both because of the rarity of the tumor and the peculiar manner in which it manifested itself.

Mrs. T., a negress, aged thirty years, a multipara, was admitted as an emergency case to the Medico-Chirurgical Maternity Hospital on November 3, 1900. Examination of the patient on admission showed her to be about six months pregnant. She complained of pain over the uterus, and an internal examination showed evidence of a threatened miscarriage. More interesting than the pregnancy was the presence of a tumor, which could be felt at the lower border of the liver. Dulness over this tumor extended into the right flank.

We were unable to elicit any previous history throwing any light upon its origin.

The patient was anemic, but had not the characteristic cachexia of malignancy. The urinalysis was negative, the temperature elevated. Five days after admission she spontaneously miscarried, giving birth to a six months' fetus.

After delivery the tumor stood out more prominently, and appeared to be rapidly increasing in size.

A tentative diagnosis of either abscess of the liver or a large growth of the kidney was made. The tumor had not the feel of a cystic kidney, nor were the clinical symptoms suggestive of liver abscess.

She still continued to have fever and was rapidly growing worse, and on November 17th was etherized and an exploratory incision made. The tumor occupied more the region of the liver, and upon deep palpation fluctuation was noticed.

An incision was made over the most prominent portion of the growth through to the peritoneal cavity; what was then found was supposed to be a retroperitoneal abscess, so gauze was packed around the wound to shut off the general peritoneal cavity, and an incision made into this bulging mass.

A large quantity of thin, dark, very offensive fluid escaped. It had the odor of urine. As the patient was in an extremely critical condition, a large drainage tube was inserted.

The abscess drained, the next day the patient seemed a trifle improved, but she commenced to lose ground again, and died December 17th, a month and a half after her admission to the hospital.

Autopsy Notes. Body of a much emaciated young colored woman of middle stature, aged about twenty-five to thirty years. The face bears an expression of suffering. Rigor mortis is absent.

Inspection of the body shows an open wound in the right hypochondrium large enough to admit a finger, and communicating with some part of the intestine, forming a fecal fistula. The edges of the wound are indurated, the surface necrotic and foul. In addition to this intestinal fistula there is a sinus which descends deeply toward the right side of the abdomen and communicates with what appears to be an abscess cavity, as puriform matter bathes the exploring finger. When closely examined this matter was curdy, and much resembled the pus of a cold abscess.

The body was opened by suitable incisions.

Thorax. Pericardium normal. Pleural adhesions on both sides. Heart: brown atrophy. No valvular lesions. Aorta normal, except for beginning atheroma. Lungs: slight congestive edema.

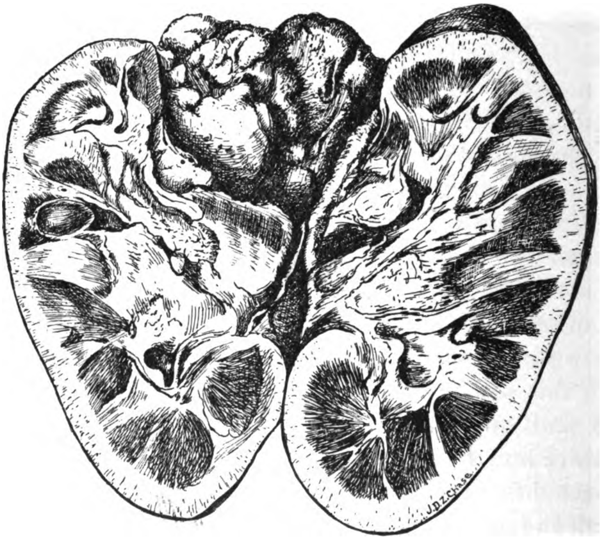
Abdomen. Chronic peritonitis, chiefly localized about the area of disease on the right side. Recent peritonitis near the external wound. Spleen: small, capsule thickened, substance indurated, vessels large. Adrenals: apparently normal. Left kidney: normal in size and appearance; on section, mild parenchymatous changes of the cortex; ureter normal. Right kidney (see below). Ureter: normal. Bladder normal. Uterus: enlarged puerperal uterus; no signs of any pathologic conditon. Ovaries: normal, Pancreas: normal, except for inflammatory adhesions to the surrounding viscera. Stomach and duodenum: normal. Small intestine: normal. Large intestine: operation, fistula communicating with the transverse colon; the transverse and ascending colon are adherent to surrounding structures by inflammatory adhesions. Vermiform appendix: normal and free of adhesions. Liver: normal. Gall-bladder: normal. Nervous system not examined. The only lesion of interest or importance is to be found in the *right kidney* and its contiguous structures.

The sinus descending from the external wound was found to communicate with a cavity above and internal to the right kidney. The appearances suggested that this cavity had once been large, but had collapsed when the external wound was made. It seemed to arise either from the kidney or the perirenal tissue. The kidney together with the surrounding perirenal tissue, forming the entire walls of the somewhat indefinite sac of the abscess (?), were removed and carefully dissected. The ureter and pelvis of the kidney were now found to be normal. Little by little the kidney was dissected free from the surrounding cellular tissue, which was thickened and infiltrated, until gradually the lower three-fourths were exposed, after which it was split longitudinally along the convex surface. The substance of the organ was now found to be free from disease—a condition which was entirely compatible with the fact that no abnormal condition of the urine was discovered during life.

Tracing down the sinus from above and laying it open, it was discovered that the inner surface of its wrinkled and contracted wall was thickly studded with more or less rounded nodules, suggesting some neoplasm. These became larger as the upper part of the kidney was approached. In the superior, external, posterior portion of the kidney there was a rounded excavation about as large as a walnut. In this excavation lay a neoplasm nearly as large as the excavation itself, and projecting so as to form a rounded mass from the bottom of the excavation into the sinus. The color of this neoplasm, as well as the color of the nodules in the neighborhood, was grayish-yellow, the surface smooth, the consistency rather firm and friable.

A section passing through the neoplasm and the adjacent kidney substance showed the tumor to be sharply demarcated from the kidney substance, being separated by a band of fibrous tissue.

FIG. 1.



Hypernephroma of the kidney. Organ split longitudinally, and showing the tumor in the upper left-hand half.

The presence of the neoplasm in the kidney, the numerous nodules in the sinus, and the absence of evidences of any inflammatory process beyond that depending upon the operation and fistula, entirely changed the aspect of the case.

It now appears as if the condition was one of primary neoplasm of the kidney with enlargement and softening. The puriform matter that escaped when the operation was performed, and continued to escape subsequently, was the softened contents of the neoplasm, enclosed in its capsule of perirenal tissue. The escape of this softened tissue was followed by collapse of the sac, and the necrosis of the remaining part of the growth with the formation of the rounded eminences found in the walls of the sinus. It was no doubt owing to this necrosis that the fecal fistula formed.

Concerning the nature of the growth the naked-eye appearances are not clear. It undoubtedly arises from the kidney, yet its growth away from the kidney substance and its sharp demarcation from it are peculiar. The growth shows no disposition to infiltrate neighboring organs or tissues, and has given no metastases. These facts seem to warrant the assumption that the growth is a *hypernephroma—i. e.*, a growth developing from a fragment of the suprarenal body included within the kidney tissue during the embryonal differentiation of the tissues.

Microscopy. The fragments of tissue were hardened in formaldehyd, embedded in paraffin, and stained for study by various methods.

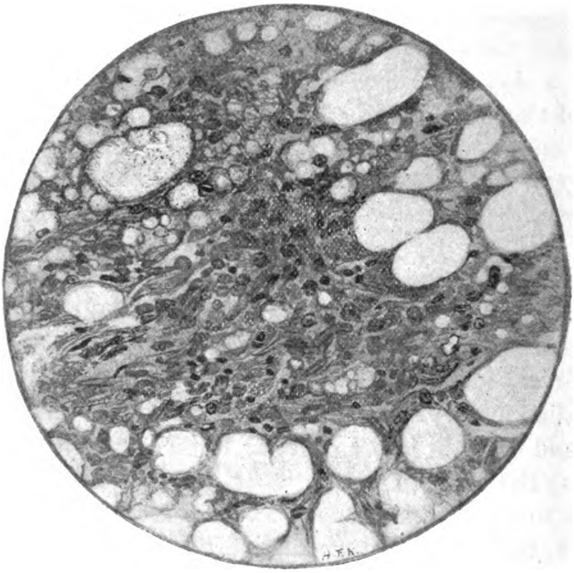
Three difficulties immediately presented themselves, and made the determination of the nature of the growth difficult. First, the entire growth was in a condition of advanced retrogressive change; second, it was evidently distinctly modified by the acute and chronic inflammatory processes that had taken place in and about it; and lastly, it was a peculiar atypical growth.

Beginning the examination with that part of the growth which is attached to the kidney, and occupies the cavity in its upper portion, we find though the largest tumor mass is firmly attached to the kidney, it does not blend with its substance anywhere, but that between the tumor tissue and the kidney tissue there is a fairly sharp line of circumscription consisting in part of a fibrous tissue belonging to the tumor, and in part of fibrous tissue resulting from atrophy of the parenchymatous elements of the organ.

The kidney structure is quite normal until the described line of demarcation is reached, when a sudden and complete pressure atrophy is observed. From the study of sections of this kind it becomes evident that the growth has not taken place from the kidney tissues.

The tissue forming the tumor is very largely in an advanced condition of *fatty infiltration* This is true not only of that part in contact with the kidney, but also of the remote parts. So widespread is this infiltration that it becomes impossible to decide upon the nature of the cells, nearly every one of which is involved in the process. Among the fatty globules thus formed, and thickly distributed in trabeculæ of fibrocellular structure, and about large bloodvessels which are present, there are cells of various kinds, most of which are unfortunately altered by degenerative change.

FIG. 2.



Hypernephroma of the kidney, showing the indefinite structure and the presence of considerable fat. This section passed through the center of the main tumor nodule. (Zeiss, Ocular II., Objective D D.)

1. *The proper cells of the tumor.* These cells are rather large, for the most part irregularly ovoid and mononucleated. They are closely packed together without any arrangement, the cytoplasm is universally injured by retrogressive changes, and contain vacuoles and granules. The nuclei were originally round, large, and vesicular, but almost every variation from the normal presents itself. There are fragmented nuclei, vacuolated nuclei,

giant pale nuclei. Occasionally a large cell with several nuclei is observed.

In general the cells bear more distinct resemblance to sarcoma cells than those of any other type, yet the extensive fatty metamorphosis and the original scanty amount of chromatin are distinctly contrary to this view.

2. *Connective tissue cells.* Spindle cells derived from the stroma of the tumor and from the bloodvessels are very numerous. Indeed, certain areas consist almost exclusively of them, their large size, arrangement in bundles, etc., forming an embryonal tissue closely suggesting spindle-cell sarcoma. These areas are, however, not numerous, and proximity to the trabeculæ, etc., from which the cells are derived, usually sufficiently explains them. Spindle cells, endothelial cells, and irregular cells evidently derived from the connective tissues and bloodvessels are scattered irregularly throughout the growth and often mingle with its proper cells.

3. *Plasma cells.* There seem to be a good many of these scattered about among the tumor cells, but their numbers are greatest in the areas in which the connective tissue cells predominate.

Leukocytes. Leukocytes occur in small numbers throughout the tumor. They are most numerous in the connective tissue areas surrounding the bloodvessels.

There is no regular framework of connective tissue supporting the cells of the tumor.

The bloodvessels are numerous, large vascular trunks more numerous in proportion than the capillaries.

Degenerations. In addition to the widespread fatty infiltration of all parts of the growth, there were numerous areas of necrosis in which no definite structure was any longer visible. Here and there, and especially in the connective tissue areas, pigmentation of leukocytes and connective tissue cells with hemosiderin was observed, but nowhere in the growth were hemorrhages found.

When other nodules of the neoplasm, from the wall of the sinus and from the perirenal tissue, were examined the advanced fatty infiltration of the cells was the most marked feature. In nearly all of these fragments the retrogressive changes were so marked that the cellular structure could not be studied.

It is evident, therefore, that the histologic structure of this tumor conforms to no regular tumor type. It is a growth attached to the right kidney and partly embedded in the fossa in the organ, yet developing from some other structure and not invading the kidney. Its peculiar cells are subject to fatty infiltration. The tendency of the growth is to increase in size without metastatic distribution, and without infiltrating contiguous structures. All of these facts seem to point to its development from adrenal tissue. It did not grow from the right adrenal itself, however, as that organ was found normally placed and reasonably normal. Therefore, if of adrenal tissue it must have been from a "rest" or fragment, misplaced and in apposition to the kidney. The preservation adopted did not permit us to determine the presence or absence of glycogen, but the facts already given, and especially the marked fatty infiltration, lead us to believe that the tumor was correctly called *hypernephroma.*

DISCUSSION.

DR. KELLY remarked that the tumor was a typical example of hypernephroma, and the first kidney referred to proliferation of aberrant adrenal rests reported in writing to the Pathological Society. This was considered somewhat remarkable in view of the fact that it was believed that most of the carcinomas and alveolar sarcomas of the kidney are in reality adrenal tumors—hypernephromas. The encapsulation of the tumor commented upon by Dr. McFarland was considered one of the characteristics of the tumor, although in advanced stages the capsule became penetrated and the tumor-growth widespread. The fat contents of the tumor cells, their arrangement into rows and double rows, their intimate association with the capillaries—a feature on which Dr. McFarland had not laid sufficient stress—and the presence of glycogen also were characteristics. It was stated that considerable attention had been directed to the presence of cysts in these tumors, and it was suggested that some of them probably owed their origin to the proliferation in later life of portions of renal tissue included within misplaced adrenal rests. Several specimens illustrating such origin of cyst formation in these tumors were demonstrated. *November* 14, 1901.

Diagnosis by Means of the Serum of the Blood: A Critical Study.*

JOSEPH SAILER, M.D.

In the past five years the study of the blood has followed lines essentially different from those pursued during the preceding decennium. The picturesque results obtained by Ehrlich's method for the differential staining of the leukocytes and the readiness with which the technic was learned, led hematologists and the medical profession in general for a long time to devote themselves almost exclusively to the study of the formed elements in the blood. In time, however, it came to be realized that the changes in these elements were pathognomonic in very few conditions, if in any; that if they sometimes contributed to a diagnosis they were, also, occasionally misleading, and, moreover, there were various manifestations in the blood that were not in the least indicated by them. The studies of immunity led to the effort to determine the changes that took place in the blood that rendered it capable either of producing disease or of preventing its occurrence, and finally to a study of the physiologic chemistry of the blood that has been of the utmost importance in the diagnosis of disease, and bids fair to be of value to therapeutics. At present the following serum reactions seem to be definitely established.

First. The reactions between micro-organisms producing infection and the serum of the infected animal. These are of four kinds: first, the agglutination; second, the solution of the micro-organisms; third, the formation of a tangled mass of motionless filaments composed of the micro-organisms, and fourth, the production of precipitates when the serum of the infected animal and the germ-free filtered culture of the bacteria are mixed.

Second. The reactions between the red blood corpuscles of one species of animal and the serum of any other species of animal into which the red blood corpuscles of the first species have been injected. These are of three kinds: Agglutination of the red blood cells, solution of the cells, and the formation of a precipitate when the serum of the animal that has been injected is mixed with the serum of an animal of the same species as that from which the blood corpuscles were taken.

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* Unfortunately it has been necessary to omit reference to a considerable number of articles on this subject on account of the immense amount of literature concerning it and the limitations in regard to space.

This paper was read as a part of a symposium upon the blood, February 27, 1902.

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Third. The reactions that occur between bacterial cultures and red blood cells. These are agglutination and solution.

Fourth. The reactions that occur between normal blood serum and bacteria. These latter are also agglutination and solution.

Fifth. The reactions that occur between the normal or diseased blood serum of certain animals and the blood corpuscles of the same or of other species. These are also agglutination, or, more frequently, solution.

Sixth. The reactions that occur between cells derived from various organs of one species of animal and the serum of an animal of another species into which an emulsion of these cells has been injected. These are generally agglutination if the cells are motile as spermatozoa, and solution if they are not motile as liver cells.

Seventh. The reactions that take place in the body when active sera, either derived from inoculated animals, or from normal animals of certain species, are injected into animals experimentally. These may be included under the term hemolysis, and are similar to the changes that occur in disease in the condition or group of conditions known by the general term pernicious anemia.

Eighth. We may discuss the production of immunity to all these various reactions.

PART I. *The Reactions Between Pathogenic Micro-organisms and the Blood Serum of Infected Animals.*

By far the most important of the clinical applications of these reactions is the Widal test, so called, that is, the reaction of the serum of persons suffering from typhoid fever with the Bacillus typhosus. Its great efficiency is now generally recognized[1] [2] even for the diagnosis of the disease in children,[2a] although it is not considered by some[3] to be an absolute test, and cases that were proven to have been typhoid fever have been observed in which the reaction did not occur,[4] [5] [6] and it is interesting to note that the reaction appears to occur with the blood of patients who have icterus,[6a] a fact that may have caused some observers to assume a relation between typhoid fever and catarrhal jaundice.[6b] * Its absence is supposed to render the prognosis somewhat unfavorable,[4] for in nonfatal infections there is an increase in the quantity of agglutinin in the blood, and, therefore, agglutination may be regarded as an early sign of a successful attempt toward protection on the part of the organism.[7] It is possible, however, that the variability of the reaction from day to day may explain some of these negative results, and, therefore, the reaction in all such cases should be made frequently.[8]

Moreover, the culture of typhoid fever should always be tested, for specimens derived from different sources may agglutinate with very variable intensity. Cultures from the bile sometimes show very slight tendency to agglutination.[9] The agglutination in high dilutions occasionally occurs in persons who have not had typhoid fever.[5] It may also be present in the children born of mothers suffering from typhoid fever,[10] [11] [12] particularly if the disease occurs during the last half of pregnancy.[13] In one instance agglutinin was found in the placental blood two months after convalescence, and in the breast milk three months after convalescence.[14] There seems to be considerable doubt regarding the tissues and fluids in which agglutinin occurs, some holding that it is formed chiefly in the spleen and lymph glands[15] and others[16] that these organs have nothing to do with it.[17] The spinal fluid, according to one investigator, possesses slight if any agglutinating qualities.[18] The urine of persons suffering from typhoid fever may have agglutinating properties.[19] The reaction does not appear to be influenced by any drugs administered to the patient;[20] it usually disappears a few months after convalescence, but has been observed in one exceptional case thirty years after infection.[21] It persists in the blood withdrawn from the patients for variable periods, as long as thirty-four days, but decreases considerably in activity.[22] There appears to be considerable difference in the reaction between agglutinated and nonagglutinated bacteria. Thus, if a guinea-pig is killed by intraperitoneal injections of typhoid bacilli, the peritoneal fluid contains bacteria that will not agglutinate unless they are cultivated

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* I have tested the blood of three patients with intense jaundice and failed to obtain the Widal reaction.

at least once artificially.[23] If typhoid bacilli are injected into the peritoneal cavity and tested from time to time it is found that they soon lose their power of agglutination. If an animal is injected with agglutinated typhoid bacilli it develops little or no agglutinin in its serum, whereas nonagglutinated bacilli increase the agglutinative power of the serum.[24] If, however, a guinea-pig is injected with agglutinated typhoid bacilli its serum acquires the power of agglutinating typhoid bacilli from the peritoneal cavity of another guinea-pig that have lost their agglutinating qualities toward ordinary immune sera.[25] The Widal reaction is occasionally valuable for the purpose of demonstrating the existence of typhoid infection in association with some other diseased condition, as for example in a case of acute tuberculosis.[26] Inoculation against typhoid fever gives rise to more agglutinin and to a greater degree of resistance if the quantity of material used is so small that it does not produce a reaction.[27]

Typhoid bacilli can be rendered nonagglutinable by keeping them for two hours in immune serum that has lost its agglutinating properties by being heated to 75° C. These micro-organisms however, may be agglutinated by the peritoneal exudate produced by the injection of bouillon containing typhoid bacilli into the peritoneal cavities of guinea-pigs. These peculiar reactions have given rise to some very complicated theories.[25a]

A large number of pathogenic bacteria have now been tested either with the serum of patients who have been suffering with the disease, or with the serum of animals artificially inoculated, in order to determine whether the agglutination reaction occurs at all, and if it does, whether it is sufficiently constant and decisive to render it possible to use it for diagnosis or for the purpose of determining the nature of the bacillus. It has already been suggested that the reaction is not entirely specific; that is to say, that the blood serum of a patient infected with a micro-organism belonging to a group might agglutinate with considerable intensity other varieties of the same group,[28] and this question is particularly important on account of the close relationship existing between the typhoid and colon bacilli. This has sometimes rendered it difficult to recognize certainly the typhoid bacilli. Thus, micro-organisms have been obtained from water that agglutinated with typhoid sera, and the serum of animals immunized to them agglutinated known typhoid bacilli, and yet they were supposed to belong to the paracolon group.[29] Others have been obtained from cadavers that showed some of the characteristics of the colon bacillus, but agglutinated with typhoid sera.[29a] Whether the colon bacillus gives any specific agglutination is a matter of considerable dispute, some authors holding that the typhoid and colon bacilli are essentially different,[30] or that the latter can be distinguished from the typhoid bacillus by agglutination in high dilution,[31] others that it is impossible to distinguish the colon from the typhoid bacillus by the agglutination test[32] [33] [34] on account of the great variability of the reaction. Moreover, the different varieties of the colon bacillus react very differently to the serum of an animal immunized to one of them, or to the serum of healthy or infected human beings sometimes agglutinating better with the serum of healthy persons,[35] sometimes agglutinating well with the serum of animals inoculated with the typhoid bacillus[36] and usually showing such great variability in the different varieties that no trustworthy conclusions can be drawn, even varieties from the same intestinal tract failing to show any constancy in their serum reactions,[37] [38] although other varieties cultivated from the blood and pus of the infected patients (newborn children) agglutinated well with the blood of those patients.[38a] Some varieties of the colon bacillus appear to be particularly susceptible to agglutination, thus, they may be affected by normal serum or by eel serum.[39] All the specific precipitates occur exactly as does the agglutination, and do not show greater constancy.[40] Among the other micro-organisms of this group for which reactions have been proven are the Bacillus mesentericus, obtained from the blood of two cases of typhoid fever and reacting with their serum,[41] and the Bacillus febris gastricæ, obtained from patients suffering from what appeared to be atypical typhoid fever,[42] which resembles in many respects the so-called paratyphoid bacillus,[42a] and reacts to the blood serum of patients infected with the latter.[42b] The bacillus of psittacosis (Nocard) appears to belong to the same group and even reacts with the blood serum of patients suffering from typhoid fever, providing the latter is only slightly diluted. The bacillus of Sanarelli and the bacillus of Havelburg are also supposed to belong to this group.[43] The latter, however, has been generally admitted not to be the cause of yellow fever. Regarding the Bacillus icteroides there is still considerable dispute. Sanarelli claims that it agglutinates with the serum of 93 per cent. of all cases of yellow fever.[44] Other investigators have only obtained positive results with such strong dilutions as 1 to 10,[45] and others have obtained the serum reaction too rarely to draw any definite conclusions.[46] The dysentery bacillus is probably also a member of the colon group. Distinct agglutination in high dilutions seems to occur, and there is strong evidence in favor of the etiologic relation of this micro-organism to at least some forms of dysentery,[47] [48] even those occurring in Europe.[48a] Shiga is, however, skeptical regarding the clinical value of the reaction.[48b]

The agglutination of the plague bacillus has also proven of value in the recognition of the disease. Great difficulty has been experienced, however, on account of the nature of the cultures of the plague bacillus, which tend to form a pellicle, that is to say, to undergo a sort of spontaneous agglutination. It is, therefore, necessary to emulsify them, which may be done either with a sodium chloride solution or after they have been dried *in vacuo*.[49] [50] [51] [51a] The reaction is usually obtained in rather strong solutions: from 2 to 1 to 40 to 1.[52] If strong it is supposed to indicate a rather mild infection.[51a] It is not so valuable in convalescence, and is not quite as trustworthy as some of the other serum reactions. With the serum of animals immunized to the plague bacillus it usually occurs promptly and in high dilutions,[52a] and may therefore be used for the purpose of testing cultures,[53] and the serum of these animals gives an abundant precipitate with the germ-free filtrate of bouillon cultures of the bacillus.[52]

Although the agglutination test with the vibrio of cholera was one of the earliest discovered, but little practical work has been done with the reaction lately, probably because cholera is no longer epidemic among the Western nations. Moreover, the number of vibrios associated with choleriform diseases is considerable, and it is not certain that they agglutinate with the serum of patients infected with other varieties. Thus, in an experimental study of this subject, made with emulsions of the pellicle or of the dead vibrios, it was found that the vibrios of

Massuah, Metschnikoff, and Finckler did not agglutinate with the serum of animals infected with the vibrio of Koch.[53a] A reaction, however, sometimes occurs with the serum of patients suffering from diseases that are probably not cholera, as, for example, with the serum of children suffering from colitis.[54] The reaction occurs either with the blood serum of infected animals[55] or with the filtrate of forty-eight-hour bouillon cultures,[56] although agglutination only occurs when the micro-organisms to be agglutinated are only slightly virulent, or with various chemical substances, such as mercuric chlorid, formalin, safranin, etc.[56] Experimentally, it has been found that the agglutinating power is transmitted from the guinea-pig to its offspring.[57]

Considerable efforts have been made in order to discover a satisfactory reaction with the tubercle bacillus that can be used clinically. Arloing and Courmant were the first to suggest this procedure,[58] using a special culture prepared in such a manner as to enable them to obtain a homogeneous emulsion. When this culture is four weeks old it is mixed with the serum in proportions of 1 to 5, 1 to 10, or 1 to 20, and the reaction is usually complete in about twenty hours. Control tubes are always necessary. The reaction is present in little less than 90 per cent. of all cases of tuberculosis, in about 35 per cent. of cases of other forms of disease, and in 27 per cent. of healthy persons. In surgical cases it appears to be absent in nontuberculous forms and present in about 77 per cent. of the tuberculous forms. It can usually be readily obtained with the pathologic exudate of tuberculous conditions. It is less likely to occur in severe than in mild cases.[59] Skepticism has been expressed regarding the nature of the cultures used by Arloing and Courmont,[60] but there appears to be little doubt now that they were working with an atypical culture of the tubercle bacillus. Experimental investigations have shown that when the tuberculous infection is severe the serum of the infected animal has little agglutinating power, and when the infection is mild the agglutinating power is considerable. The reaction is therefore of diagnostic value only when positive, and its absence does not exclude tuberculosis.[61] The blood serum of persons suffering from tuberculosis appears to have considerable agglutinating power for a variety of micro-organisms in addition to the tubercle bacillus. Nearly all writers have found the reaction exceedingly variable,[62] [63] [64] or else negative[65] even with the fluid from a lumbar puncture.[66] In fact, it can hardly be said to be a specific reaction.[68a] Koch has performed some very elaborate experiments with it, obtaining a homogeneous emulsion by gradually triturating the bacillus with a 1-50 normal soda solution, centrifugating and diluting with a weak HCl solution until the reaction is faintly alkaline. It is then further diluted with carbolic acid and physiologic salt solution until the proportion is 1 part of dried culture to 3000. This emulsion will last about two weeks. The dilution of the serum should be from 1 to 10 to 1 to 300. In human beings it is usually necessary to employ stronger solutions, 1 to 10. Upon animals the results were variable, but it was found that the methods for producing immunity caused an increase in the agglutinating power of the serum. Koch does not believe that it is of value in diagnosis, but thinks that it may indicate to a certain extent the degree of immunity obtained by the individual, and it seems to prove that up to a certain extent protective substances are formed in persons suffering from phthisis.[67] Homogeneous cultures may also be obtained by shaking bouillon cultures daily. It is interesting to note that it has been determined that Maragliano's serum agglutinates the tubercle bacillus and Koch's tuberculin will not.[64]

The agglutination of the pneumococcus has also been tested very elaborately, the method being to inoculate tubes containing blood serum obtained from a patient suffering from pneumonia.[68] The cultures must have recently passed through the body of an animal, and it is found that as the crisis approaches the cultures show more and more tendency to agglutinate and to sink in masses to the bottom of the tubes. The reaction must be made in the incubator, and is complete in fifteen or sixteen hours. It is rather more satisfactory if the micro-organisms are obtained from the patient than from a laboratory culture.[68a] When examined, the micro-organisms show the capsules with exceptional distinctness. Dilution, even of 1 to 2, interferes with this reaction. The reaction appears to be particularly valuable in cases of pneumonia complicating some other disease, as, for example, typhoid fever.

Malta fever also gives a typical reaction which has been confirmed a number of times.[70] [71] It occurs in high dilutions and persists for months after convalescence. The bacillus of glanders agglutinates with the serum of infected animals in very high dilutions. In fact, it is doubtful if the reaction is characteristic unless the dilution is more than 1 to 400.[72] The Bacillus pyocyaneus agglutinates with the serum of immune animals in dilutions of 1 to 50 or 60, or even more, and there is evidence that the agglutinin is formed in the infected organisms because it is not present in the culture.[73] [74] The Proteus vulgaris will agglutinate with the serum of an animal infected with the culture used in the test, but agglutination of other varieties does not appear to occur. This simply proves the diverse nature of the different varieties of this germ. It has been claimed that agglutination has been obtained with the bacillus of leprosy, although it has never yet been satisfactorily demonstrated that cultures of this organism have been grown. The doubtful cultures, however, gave a reaction with the serum of certain cases of leprosy in dilutions as high as 1 to 1000.[75] It is doubtful whether the tetanus bacillus actually agglutinates. With the serum of some normal animals a slight agglutination may occur which can be very slightly increased by the injection of antitoxin. Infection with the tetanus bacillus appears to have no effect whatever in increasing the agglutinating power.[76] Even the blastomycetes are susceptible to this reaction, and agglutinate with the serum diluted as much as 1 to 50,000. Other varieties may agglutinate with the specific serum, although not quite so actively. The yeast cells are apparently not destroyed.[77] [78]

It is only natural, in view of the considerable amount of experimental work done upon agglutination, that a large number of theories should have been suggested to explain it. No one of these theories has as yet been established by a sufficiently complete series of accurate observations to enable it to obtain general credence, and the problem can therefore be said to be still unsolved. A certain number of facts have, however, been demonstrated, that will probably serve when they are sufficiently amplified and increased, to indicate the real nature of the process. In the early days of the Widal reaction there was considerable dispute as to whether the reaction was one of immunity or infection, Widal, himself, inclining strongly to the latter opinion. The nature of the reaction with micro-organisms other than the bacterium typhi has seemed to indicate very strongly that the reaction is really one of immunity; but of late there is some reason to believe that it is partly physical and partly chemical. It is now known, for example, that the severity of the infection has little influence upon the degree of agglutination. Lethal doses do not prevent the reaction and nonlethal doses increase it variably in different animals. But this increase is not proportionate to the degree of immunity, although the increase during the progress of a disease may be regarded as evidence of the successful production of immunity on the part of the organism.[79] There is much reason to believe that the agglutinating substances are of different nature from the bactericidal substances of the serum.[80] In fact, it is possible for animals to develop agglutinative substances in their blood serum without developing protective bodies, and when both agglutinative and immunizing substances are produced, the former usually disappears first.[81] Considerable confusion may arise in the study of this subject from the fact that there are different forms of agglutination, four varieties at least being recognized, although only two of these are sufficiently characteristic to be considered true reactions; that is, those in which there is clumping and loss of motility.[3] In regard to the mechanism of agglutination the evidence is still rather unsatisfactory. We know that freezing the serum does not destroy the agglutination reaction;[83] that the abstraction of salts from the serum by dialysis prevents it completely,[84] and that the partial withdrawal of salts diminishes or inhibits it considerably.[85] The question whether it is a vital or purely chemical process still remains undecided. Some investigators hold that the agglutinin is really an enzyme, and they give to it the name of the bacteria with the suffix "ase," as, for example, pyocyanase.[86] Others call attention to the analogy between the active sera and the digestive juices.[87] Others, still, distinguish between the so-called specific and nonspecific agglutinins, the former being merely a precipitation of all the coagulable bodies in the culture media, the latter the precipitation of the active bodies alone.[88] The micro-organisms perhaps play a merely passive rôle. One authority goes so far as to state that in agglutination there are two stages, first, in which the specific substances unite with the salts, which is purely chemical; second, in which the microbes unite in clumps and form a precipitate in the bottom of the vessel, a process that resembles chemical precipitation in all respects.[89] A fact of considerable importance in this subject, although its true significance has not been entirely determined, is the discovery of specific precipitates upon the addition of immune sera to the filtrate of a bouillon culture, a reaction that can also be obtained by placing specific sera above gelatine cultures.[90] This reaction, of course, resembles that between the blood sera of two species of animals, one of which has been immunized to the active serum of the other, a reaction that will subsequently be described. The theory has long been held by Grüber, Paltauf, and others that agglutination was due to a change in the capsules of the bacteria, whereby they became sticky, adhered, and then, losing motility, fell to the bottom of the vessel. A modification of this theory was made by Paltauf, after the discovery of the specific precipitates by Kraus. He believed that a coagulum was formed in the liquid media in which the microbes were entangled and mechanically massed together. Others supposed that the agglutinable substance was formed by a reaction between the fluid and the peripheral portion of the microbes, so that they were massed together;[91] but little actual experimental work has been done on this subject. A series of experiments with typhoid bacilli showed that agglutination was abolished after the outer layer of the microbes had been dissolved by the action of pyocyanase, even in micro-organisms that reacted in a dilution of 1 to 2,000,000. Partial solution served to diminish the reaction. The reaction was restored after total solution if some filtered culture were added to the mixture of bacteria and serum. It therefore seems likely that the agglutinating substance exists in the outer layer of the bacteria, and it is possible that it may be partly dissolved in the culture media.[92] A modification of this theory is that the agglutinating substance is formed particularly upon the cilia of the micro-organisms,[93] a hypothesis that appears to be disproved by the facts that non-ciliated bacteria often give an excellent reaction and that red blood cells and other cells of the body may also give atypical agglutinative reactions.[94] On the other hand, it has been claimed that the process is due to the action of a ferment or enzyme.[94a] There seems to be no doubt that in some way the substance of the bacteria is altered, and that this alteration is not a vital phenomenon because it can occur in dead as well as in living micro-organisms. In fact, in some cases, as for example in the case of the tubercle bacilli, dead micro-organisms appear to react better than living ones. This change is evidently brought about by the action of immune sera, which apparently renders the bacteria more susceptible to the action of certain other substances in the serum that resemble the alexins.[95] The change can also be produced by other non-specific substances, particularly certain stains, such as saffranin. Although the process bears a superficial resemblance to chemical precipitation, and also to coagulation, there is no sufficiently definite evidence to prove that it is identical with either of these. A modification of agglutination to which sufficient attention has not hitherto been directed is the formation of filaments in the cultures of the bacteria. This has been particularly observed by Kraus, and appears to resemble a vital phenomenon more than the ordinary massing in clumps.[96] In regard to the hypothetic substance by which agglutination is brought about, particularly the so-called agglutinin, it has never yet been isolated, although it has been claimed that it is possible to separate it in an impure state from the specific sera,[97] but at present too little is known about it to enable us to draw any conclusions regarding it excepting that in its reactions to heat it bears some resemblance to ferments, and that at least two substances are necessary in order to manifest this action. At present it is well to follow the advice of Gruber and refrain from giving it any name that presupposes a separate identity.[98]

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Exencephalic (Iniencephalic?) Monster with Bilateral Harelip and Cleft Palate.

ELLIS E. W. GIVEN, M.D.

The monster which I wish to present this evening is a seven months' white female fetus, which was stillborn, being the first child of an extremely neurasthenic woman of seventeen and a half years, whose family history I cannot obtain, but whose pregnancy up to the time of the miscarriage was uneventful. The father is about twenty-five years of age, healthy and robust, but having a strong family history of tuberculosis, his father having died of phthisis, and his mother is now suffering with the same disease.

About one week before the miscarriage the mother fell directly forward upon her abdomen, followed by severe lumbar pain and uterine hemorrhage, but continued to feel fetal movements up to within two days of the birth. Hydramnios was not present, as has been frequently reported in cases of this malformation, and labor was not long or severe.

Following the classification of Isidore Geoffroy Saint Hilaire, whose work upon *Teratology* has practically been accepted and followed by all writers upon this subject, this monster belongs in the general class of exencephalus, which is described as "characterized by a malformed brain, situated, at least in part, without the cranial cavity, the bony walls of which are themselves imperfect." This general class is further subdivided into the (1) Notencephalus, in which the cranial contents are in large part without the skull, resting upon the back of the neck, the tumor protruding through a fissure or aperture in the occipital bone. This deformity is usually associated with hydrocephalus of greater or less degree. (2) Proencephalus, in which the same deformity as just described exists upon the anterior portion of the skull. (3) Podencephalus and (4) Hyperencephalus: in these the cranial deformity is upon the vertex, and the tumor protrudes from above, the podencephalic differing from the hyperencephalic only in degree. (5) Iniencephalus: in this subclass the deformity of the skull is the same as in notencephalus, with the addition of a spinal cleft of varying degree. In some cases the failure of union extends as far downward as the coccyx, leaving the spinal canal open throughout its entire length. In this class lordosis and compensatory kyphosis are common; the head is tilted strongly backward, causing the face to look almost directly upward, which, with the faulty development of the vault of the cranium and apparent, rather than real, protrusion of the eyes, has suggested the term "frog-faced" monster, although this term is not exclusively applied to the iniencephalic subclass.

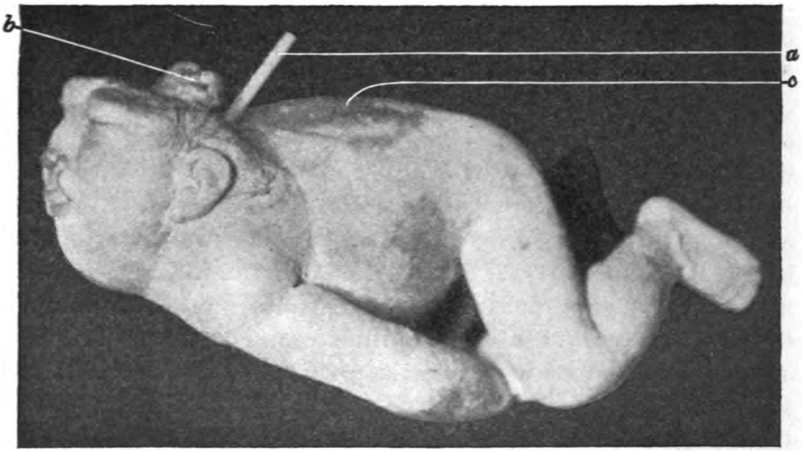
In 1896 Dr. H. F. Lewis presented a specimen of this monstrosity to the Chicago Pathological Society, and at the same time collected all the recorded cases, which with two other specimens he described at the same time, and which had not previously been recorded, brought the total number to twenty-five. I have been able since that time to find reports of only four other cases, although the search through the records has been cursory rather than exhaustive.

No mention could be found in any of the recorded cases of an associated harelip or cleft palate (unless the case described by Dr. Wood could be looked upon as an attempt at harelip formation), with the exception of a single outline sketch in Ahlfeld's *Atlas*, which quite closely resembles the photograph of the present specimen.

The present specimen is an underdeveloped female fetus, skin and visible mucous membranes normal. The neck is entirely absent, the malformed head being placed directly upon the upper portion of the thorax in such a position as to turn the face directly upward, so that the plane of the face is at a right angle to the plane of the body, and to cause the deformed or underdeveloped occipital bone to rest directly back upon the anteriorly curved cervical vertebræ. (See photograph.)

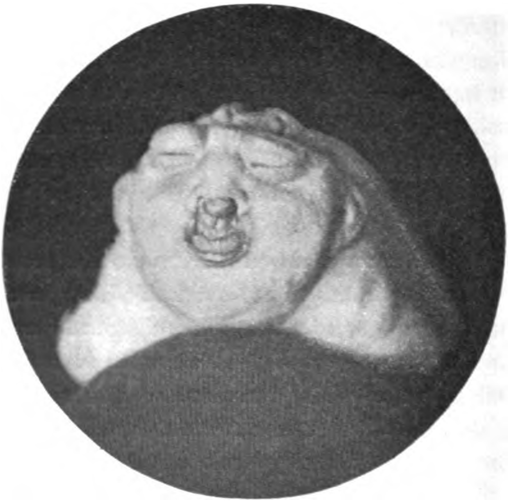
The entire upper portion of the skull, above an imaginary plane beginning on a level with the superciliary ridges and passing backward at a right angle to the plane of the face, is entirely absent,

FIG. 1.



The general appearance of the monster. The match-stick (*a*) has been passed into the opening in the malformed brain cavity; (*b*) the remains of the brain, meninges, and fringes of skin rolled up as a ball; (*c*) area over which there was failure of development of true skin. The constriction about the upper portion of the thorax and the arm was produced by a tight string used to suspend the fetus in the preserving fluid.

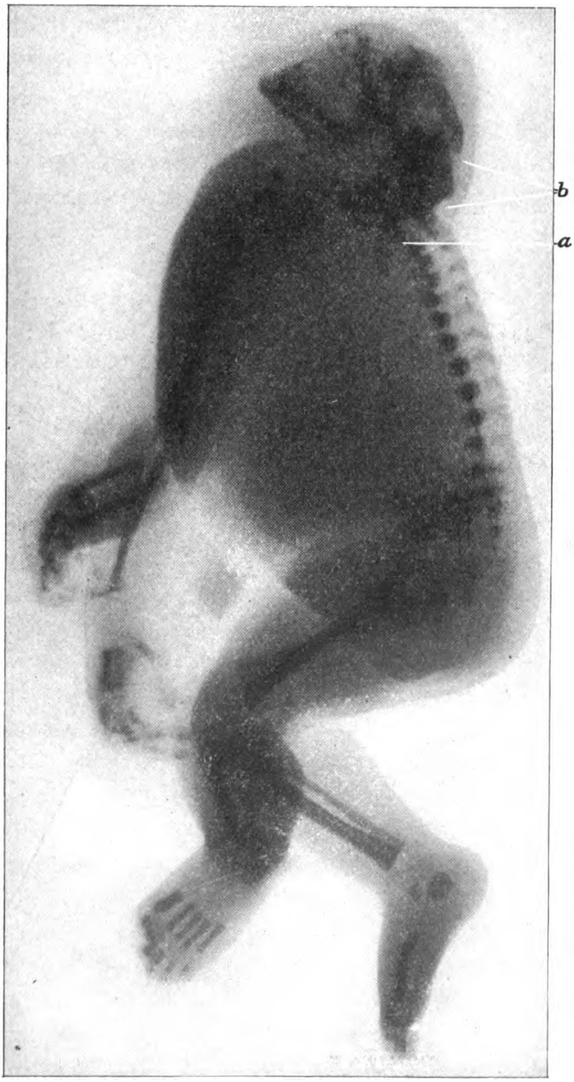
FIG. 2.



Photograph of monster, showing the characteristic formation of the face, and in addition the bilateral harelip, with the greatly protruding intermaxillary bone. The two white spots seen just below the center of the tongue were caused by moisture on the lip at the time the photograph was taken.

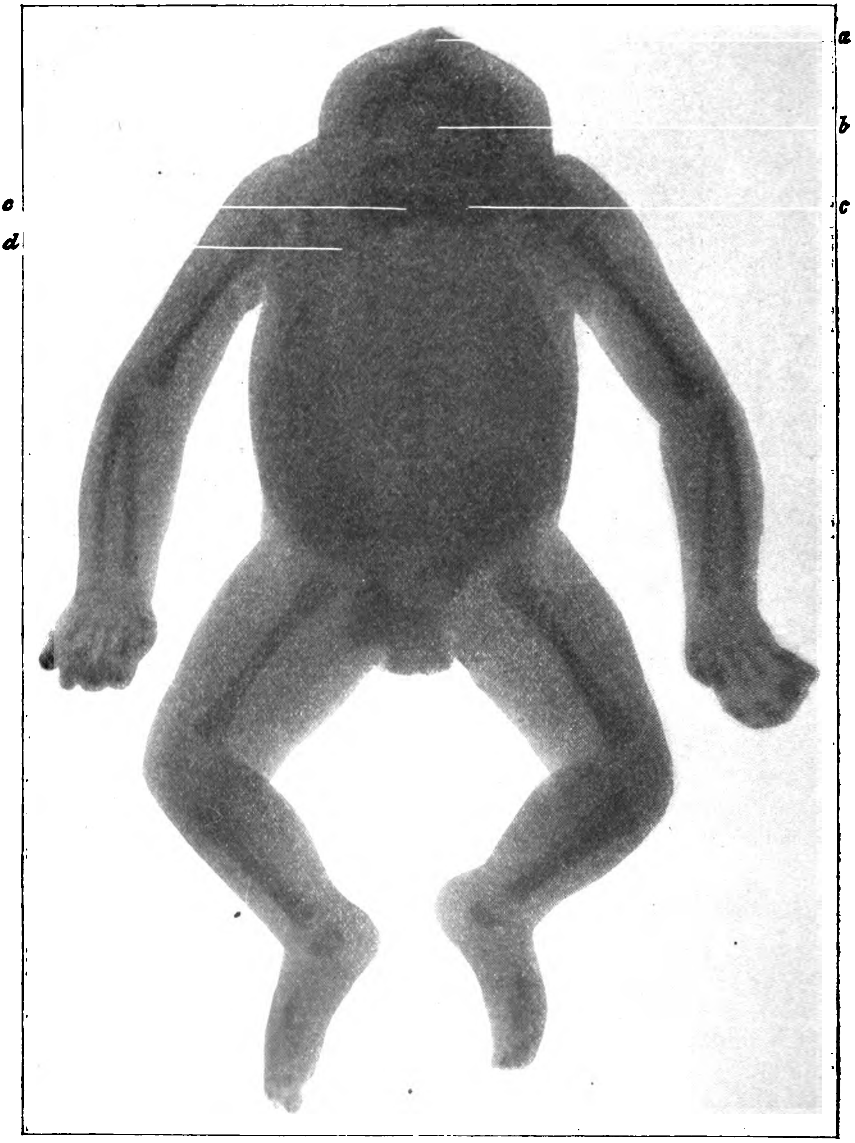
and replaced by a solid bony plate, covered by hairy skin. At the junction of the occipital bones and spinal column is an opening

FIG. 3.



"X-ray" photograph, showing (*a*) the characteristic cervical lordosis. The remains of the brain and meninges appear as the faint shadows surrounding the optical bones (*b*).

FIG. 4.



"X-ray" photograph, showing (*a*) the protruding intermaxillary bone; (*b*) failure of union of hard palate; (*c c*) abnormal position of malformed and separated optical bones; (*d*) scapula and scoliosis.

into the skull large enough to admit the end of one's little finger (in the photograph is shown a match-stick passed into the opening); from the margins of this opening are extending the brain membranes and remains of the brain, together with fringes of skin (in the photograph these are seen rolled up as a ball).

Extending over the back from the opening into the skull to the lower lumbar vertebræ, and laterally about 2.5 cm. to each side of the spinal column, is an area over which the skin has not grown, the tissues being absent down to the muscular structures, through which the ribs and closed spinal column can plainly be seen. This is not an area of abrasion, as at first appears, but one devoid of true skin. The distance from the opening into the skull to the coccyx is 10 cm.

The ears, so far as can be seen, are normally developed, and are behind and slightly below the shoulders. They are 2.5 cm. long and 1 cm. wide. The eyes are normally located and appear normally developed, the palpebral fissure measuring 1.5 cm., and the distance between the inner canthi is 1.5 cm.

The mouth, which is 2 cm. wide, is the seat of a well-marked bilateral harelip, the cleft on each side extending well up into the nostril of the corresponding side, the intermaxillary bone being quite prominent. The bony cleft extends backward into the mouth, and involves both hard and soft palate to a considerable degree. The distance between the alæ nasi is 1.5 cm. The tongue is quite large and prominent, protruding from the mouth. With the exception of the above noted abnormalities the fetus is normal.

Synopsis of Collected Cases.

CASE I. (Case of Dr. Albert C. Bowerman.)—Patient, aged twenty-four years, gave birth, about two years ago, to an apparently normal child, but it died in ten months, of some cerebral trouble. Present pregnancy advanced to eighth month. Hydramnios present. Female fetus, weighed three pounds, lived about one hour. Body and limbs fairly well developed, though somewhat disproportionate, lower limbs especially long. No neck. Ears well developed, and are behind and rather below shoulder joints; face well formed and directed upward, eyes prominent. Cranium open in occipital region and continuous with the unclosed spinal canal as far down as the lower lumbar vertebræ. Protruding from the upper end of this canal were the congested lobes of the cerebellum, much enlarged and exposed across the base of the sacrum. Length of back from occiput to sacrum not over three inches. Child had appearance of crescent, with the hollow at the back.

CASE II. (Case of Dr. B. Onuf.)—Duplicity of the face and the anterior part of the head; the duplicity begins proximally from the petrous portion of the temporal bones, including the sphenoid, frontal, nasal, supramaxillary and inframaxillary bones. Two pharynges are present which communicate with each other. Craniorrachischisis involves the entire vertebral column.

There is the interposition of a peculiar os-sacrum-like vertebral formation and two longitudinal bones (each divided into anterior and posterior portion) between the occipital and temporal bones of each side. In the proximodistal direction these intercalary formations form the transition between the bones of the skull and the vertebral column. There is also absence of the bony sternum.

CASE III. (Case of Dr. W. Atkinson Wood.)—Mother aged twenty-three years, father aged twenty-six years. Female fetus born dead, but the tissues appeared healthy and fresh. Entire scalp from the superciliary ridge to the position of the occipital protuberance and from one mastoid region to the other was a mass of dry gangrene studded with pear-shaped fibrous outgrowths. Both eyes protruded markedly and the mouth in the mid-line was quite absent, being represented by two lateral slits into which a probe passed easily for half an inch. Both ears were well developed. At the third or fourth lumbar vertebra was a myelocele. The lower extremities were fully flexed at the hips, so that the feet, which were in the position of talipes spasticus or dorsalis, were fitted and pressed accurately under the position of the chin.

The vertex was removed on a level with the superciliary ridge, and the bones were so fused together as to appear as one bony mass. The petrous portion of the temporal bone and mastoid bones were fused into one mass; on the inner side of this mass were two cavities containing brain-matter, each about the size of a bean. In the substance of these bony masses the ossicles were well developed. The sphenoidal cells were well developed, and the nasal chambers connected directly with the anterior fossa of the skull.

The vertebral column had no direct communication with the skull, being kept in apposition only by skin and connective tissue. The spinal canal opened directly at the depression on the posterior part of the skull, the spinal cord being thus exposed to the air.

The pharynx and larynx were well developed. Tongue and tonsils were contained in a membranous sac on the anterior surface of the spinal vertebræ. The internal carotid was doubtfully developed (which the author ascribed as the probable cause of the cranial deformity).

The lower and upper jaws were ankylosed together; the buccal cavity was divided into two lateral halves. The alveolar processes of the upper jaw were fused with the hard palate, leaving a slit-like opening between.

Case IV. (Case of Dr. Barton C. Hirst.)—The doctor presented a photograph of the monster, with no description.

The specimen shown this evening will be presented to the Wistar Institute of the University of Pennsylvania.

I am indebted to Dr. Clifford B. Farr for the translations of the foreign references, and to Dr. Thomas S. Stewart, who furnished the X-ray negatives.

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February 13, 1902.

A Case of Combined Aortic and Mitral Disease.

JOSEPH SAILER, M.D.

(*From the University Hospital, Service of Prof. Musser.*)

The study of heart disease is rendered more difficult by the fact that the mechanical conditions in the heart appear to be so simple that we can determine the nature of lesions by *à priori* reasoning. But it is only the association of careful clinical study and postmortem examination that enable us to arrive at any definite conclusion, and not infrequently in a series of cases studied in this way the conclusions will appear contradictory. The following case is an illustration of the fact that certain of the criteria upon which we depend for the diagnosis or exclusion of multiple valvular lesions are not invariably trustworthy.

The patient, a man twenty-five years of age, had been troubled with some heart disease since an attack of typhoid pneumonia twelve years ago. This trouble consisted of palpitation upon exertion. Dyspnea commenced two years ago. Five days before admission he had had a chill, and for two weeks had had morning cough, with slight expectoration. He was a moderately well-developed male; no edema or cyanosis. There were all the characteristic vascular signs of aortic regurgitation; the heart was enormously enlarged to the left, but absolute dulness did not extend beyond the left border of the sternum. There was a loud blowing systolic murmur at the apex, which decreased at the fourth interspace, and then became louder, reaching its maximum intensity at the right clavicle, and being distinctly transmitted into the carotid and subclavian arteries. The diastolic murmur was loudest at the third rib, and was transmitted down both sides of the sternum. The lungs, aside from harsh vesicular respiration, were apparently normal.

After remaining in the hospital for four weeks the patient had a chill, and the temperature rose to 104°. It remained elevated for six days, after which time it rarely exceeded the normal point, although it was frequently subnormal. During the febrile attack the leukocytes, which had been 8000 on admission, reached 18,000, and afterward 26,000. The patient had profuse expectoration. Seven days before his death he developed jaundice, which rapidly became intense, and he died eighteen days after the initial chill. At the autopsy the interesting features were the condition of the heart valves and the explanation of the jaundice. During life, in view of the existence of the Corrigan pulse, the absence of enlargement of the heart to the right, the absence of any sign of pulmonary congestion when the patient was admitted, and the absence of edema of the extremities, a diagnosis was made of aortic regurgitation, with dilatation of the ascending portion of the aorta, and it was supposed that the mitral valve was competent. At the autopsy the following conditions were found: The external layer of the pericardium was adherent to the right lung at the diaphragm on the right side; the heart was enormously enlarged, weighing 1150 grams; the right auricle was slightly distended; the tricuspid valve admitted three fingers; the wall of the right ventricle was about twice as thick as normal, and the cavity was increased in size; the left ventricle was distended, and the walls were thinner than normal. The posterior leaflet of the mitral valve was replaced by a slightly elevated piece of scar tissue, and the anterior leaflet was greatly thickened, and there was an atheromatous ulcer, with calcareous infiltration at the septal end. The aortic leaflets were also greatly thickened, and there were calcareous masses in the sinuses of Valsalva. Tried by the hydrostatic test the aortic and mitral valves were absolutely incompetent. The aorta showed a slight degree of atheroma, but otherwise was practically normal. The right lung showed complete pulmonary consolidation. At the apices of both lungs there were some old, partially calcified tubercles. The liver was slightly enlarged; the gall-bladder was distended with dark fluid bile; all the ducts were freely patulous.

Stress has been laid, particularly by Thayer and Tyson, upon the value of the Corrigan pulse in excluding mitral stenosis in cases of aortic regurgitation in which the Flint murmur is present, and in one case of mine upon which an autopsy was obtained it proved of distinct value. In two other cases of aortic regurgitation that were under my observation, and upon which autopsies were also obtained, the presence of the Corrigan pulse and the absence of enlargement of the heart to the right led to a correct diagnosis that the mitral valves were not involved, although in both cases a loud systolic murmur could be heard at the apex. It is difficult to understand why, with apparently similar symptoms this was not true in the present case. It is, of course, possible to speculate regarding the value of a compensatory hypertrophy of the right ventricle, which in this instance was apparently present, but that does not suffice to explain why, upon admission, there were no signs of pulmonary congestion. The case merely serves to show that mitral disease may co-exist with a typical Corrigan pulse, and that in this case the oscillation was rather more than normal was shown by some tests made by Dr. Stanton with the Oliver tonometer. The only satisfactory cause found for the jaundice was the pneumonia present in the right lung. It is interesting to note that in the last twelve days of the patient's life the temperature was practically normal or subnormal in spite of the large extent of the inflammatory process and the presence of a high leukocytosis.

In conclusion, I desire to state that when the patient was admitted he was carefully studied by Dr. A. O. J. Kelly and myself, and I also desire to express my thanks to Dr. John H. Musser for his permission to publish this case. *May* 22, 1902.

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Pathological Society of Philadelphia.

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Report of a Case of Splenic Pseudoleukemia.

THOMAS G. ASHTON, M.D.

(Pathologic report by A. F. COCA, M.D.)

Although the pathologic findings in the present case are of paramount interest, the clinical history is, nevertheless, not without importance.

The patient, Antonio De G., a native of Italy, aged twenty-eight years, entered my wards in the Philadelphia Hospital on February 10, 1902, complaining chiefly of pain in the left abdominal region, weakness, headache, and anorexia.

The family history has no bearing upon the case, his father and three brothers dying of some acute disease, each after a few days' illness, while his mother is still living, and well.

The patient had been in this country for five months, having previously lived in the northern part of Italy, where he pursued the occupation of a laborer, chiefly as a worker of the ground. Alcohol and tobacco had both been used to excess, but any venereal history was denied.

No history of a previous illness could be obtained, with the exception of an attack of chills and fever seven months preceding his admission to the hospital, and while the patient was still a resident of Italy. With this attack he was ill one week, the ague yielding readily to treatment, and though it was probably caused by a malarial infection, it was attended by urgent vomiting and pain over the splenic area, symptoms that were prominent features of his case while under our care.

Nevertheless he remained subjectively in perfectly good health until the middle of January of the present year, or about four weeks before first coming under our observation. At that time he was taken somewhat suddenly ill with general pains, fever, but no chilliness, and marked distress over the region of the spleen.

While in the hospital these symptoms persisted, and were superadded to by diarrhea, intractable vomiting, anorexia, loss of weight, profound asthenia, and headache; while a mild cough with occasional blood-tinged expectoration had existed for about two months. The case pursued a febrile course throughout, the temperature being of an irregular type.

The physical examination showed a considerably emaciated adult male, with a muddy or slightly icteroid hue to the skin and an anxious expression. The mucous membranes were pale; the tongue thin, coated, and extremely pale, and a herpetic eruption about the lips. The eyes were sunken, the conjunctivæ pale and slightly tinged with yellow, the pupils reacting normally.

Visible pulsation of the vessels of the neck was observed. The pulse was regular but rapid and compressible. The apex-beat of the heart, although not visible, was found upon palpation to occupy its normal position. At the apex a soft systolic murmur was heard, but was not transmitted, and a faint systolic murmur was also detected at the left base over the pulmonary area.

The lungs generally were hyperresonant except over the right upper lobe anteriorly, where the percussion note was less resonant, and where at the necropsy extensive pleural adhesions were found.

Numerous subcrepitant and submucous rales were heard throughout, being especially numerous at the bases.

The abdomen was greatly enlarged, particularly on the left side, due in great part to a marked increase in the size of the spleen. The area of splenic dulness extended in the anterior axillary line from the sixth intercostal space to a point one inch below a line drawn transversely through the umbilicus. The anterior border passed forward as far as the umbilicus and above merged with hepatic dulness; it presented two distinct notchings. Palpation of the spleen caused much distress. Immediately below the costal border over the spleen a distinct blowing murmur could be heard.

Liver dulness in the right mammillary line began above, in the fifth interspace, and extended about two inches below the costal margin, the left lobe also showing some increase in size. Palpation of the liver caused no tenderness.

The superficial lymphatic glands were not enlarged, and there were no symptoms of involvement of the nervous system; neither at any time were there any hemorrhagic manifestations. Extreme tenderness of the sternum and tibiæ was present.

An ophthalmoscopic examination made by Dr. Oliver showed marked neuroretinitis in both eyes, and aggregates of leukocytes and areas of partially absorbed erythrocites, most pronounced in the region of the disks and maculæ. The retinal veins were engorged and the eye-grounds extremely pallid. Conjunctivæ blanched.

Examination of the urine gave a specific gravity of 1012; acid reaction; no sugar; a decided amount of albumin. Microscopically, coarse granular and granular epithelial casts were found.

Examination of the sputum for tubercle bacilli gave negative results.

The blood examined first on February 12th, the second day after the patient's admission, showed the erythrocytes to number 1,610,000; the leukocytes, 5600, and the hemoglobin to be 20 per cent. The erythrocytes were much deformed, and there were numerous microcytes and macrocytes. No nucleated cells were present. On February 15th the blood count was substantially the same; the hemoglobin, however, had fallen to 16 per cent.

Differential estimation showed the leukocytes to be made up as follows: Polymorphonuclear, 58 per cent.; large mononuclear, 21 per cent.; small mononuclear, 14 per cent.; transitional forms, 3½ per cent.; eosinophiles, 3½ per cent.

The final blood count was made on February 24th, and showed a decided falling off in the number of erythrocytes, the number then being 1,100,000; leukocytes, 5800, and hemoglobin, 16 per cent. The differential count of the leukocytes showed no material change from the previous examinations.

On February 26th the patient died.

Pathologic Findings. The autopsy of this case was performed by Professor Flexner, to whom the writer is indebted for the privilege of reporting it. His report is as follows:

Autopsy held five hours after death. Body of slightly built, emaciated male. Pigmented surface, sallow. No edema. Pigmentation slightly more marked over pubes. Mucous membranes pale. Pupils equal and moderately dilated. At the outer side of the right foot is an old scar. Abdomen moderately distended. No rigor mortis. Subcutaneous fat slight. Muscles pale; omentum free; small amount of fat; 60 c.c. of serum in abdominal cavity.

Liver free from adhesions; 7 cm. below costal margin on right side; 6 cm. on left; 9 cm. below ensiform cartilage. *Right lung* bound; left lung free; in each pleural cavity 200 c.c. of clear fluid. *Pericardium* contains 40 c.c. of clear, yellow serum; both layers smooth; visceral layer edematous. Heart valves normal; heart flesh pale and friable. *Left lung* does not retract; is pale and generally emphysematous. *Right lung.* Upper lobe posteriorly shows congested area, triangular in shape, 2 x 3 cm., showing appearance of infarction. *Spleen* much enlarged, extending to line drawn transversely across abdomen at umbilicus. Weight, 2000 grams, bound to diaphragm and abdominal wall. It is very firm; on section, it presents uniform brownish-red color. *Liver* is smooth, of rusty brown color; on section, uniform rusty brown color. *Pancreas* is firm and gray. *Kidneys.* Capsule strips easily; mottled; cortex swollen; striæ pronounced; pyramids injected. *Adrenals* small, but apparently normal. *Stomach.* Mucous membrane is soft; otherwise normal. *Small intestine.* Mucous membrane pale. *Large intestine.* Mucous membrane much congested. *Bone-marrow* (femur) is red, soft, lymphoid. *Larynx.* At conjunction of cricoid and thyroid on left side is an area of necrosis, 2 x 2 cm., extending into the cartilage, which is dark and gangrenous. *Left tonsil* shows circumscribed swelling the size of a bean; surface congested. *Gastrohepatic lymph glands* swollen and of rusty brown color. Remaining lymph glands not prominent. On both sides of the dura mater are found petechial ecchymoses.

Pathologic Diagnosis. Grave anemia; chronic splenic tumor; pigmented liver; gastrohepatic lymph glands; lymphoid bone-marrow; pulmonary emphysema and lobular hepatization; swelling of left tonsil; circumscribed necrosis of larynx; petechial ecchymoses on both sides of the dura mater.

Bacteriology. Cultures from liver, spleen, and kidney remained sterile after a week's incubation.

Spleen. The capsule is considerably thickened, but otherwise normal. There is a marked increase in the splenic pulp in the amount of connective tissue of both the white fibrous and elastic varieties. The Malpighian bodies are generally sclerosed, the process often being most marked in the immediate neighborhood of the bloodvessels. The walls of the latter are hyaline. Hyaline flakes are found in a few of the Malpighian bodies, collected in longitudinal masses. The blood sinuses are congested and contain many red cells, which stain poorly or not at all; also mononuclear eosinophiles, lymphoid cells, and large cells with multilobulate nuclei identical with those found in bone-marrow. Numbers of cells are found containing spherical hyaline acidophilic bodies, measuring from 1 to 10 μ in diameter. These bodies are also found in small collections, lying free in the spaces of the splenic reticulum. No normoblasts are found. A number of karyokinetic phases occur in cells of the splenic pulp. Many large cells with large single vesicular nuclei and prominent nucleolus are caught in the act of ameboid movement. The protoplasm of these cells is abundant, and, with hematoxylin, take a purplish tint.

The wall of one of the large splenic vessels is broken through in two places, and the lumen invaded by tissue continuous and identical with the splenic pulp. Immediately beneath the endothelium of this vessel is found a layer of lymphoid and red blood cells.

Bone-marrow. Smears stained by Jenner's method show nothing abnormal. Sections show complete absence of fat and increased numbers of the normal cellular elements, especially of mononuclear neutrophiles and eosinophiles, but no noticeable increase in the number of either normoblasts or lymphoid cells. No megaloblasts are found.

Lymph Glands (gastrohepatic). The connective tissue in the glands is increased; no karyokinesis is observed. The hyaline acidophilic bodies described in the spleen are found in the same situations here. There is a marked dilatation of the efferent lymphatics, in which pigment-bearing cells are found. Two are *hemolymph* glands with typical peripheral blood sinus, in which are found nucleated red cells, marrow cells, and the multilobulate cells of bone-marrow. Mast cells are absent. A coarsely granular golden-yellow to yellowish-brown iron-bearing pigment is found: 1. In large cells with oval, reniform, or rounded and usually eccentric nuclei, and possessing abundant protoplasm, lying unattached in the reticular spaces. The nucleus is frequently concealed by the abundance of pigment. 2. In the proper cells of the reticulum. 3. Lying free in the substance of the reticulum itself and in the reticular spaces.

Liver. The hepatic cells are generally swollen, and show early fatty metamorphosis, this being most marked in the neighborhood of the hepatic vein. The capillaries are greatly dilated, and contain an abnormally large proportion of lymphocytes and a few mononuclear eosinophiles and neutrophiles. One multilobulate marrow cell is found. No nucleated red cells. Connective tissue not increased. Capsule normal. Numbers of mast cells are found in the connective tissue of the interlobular spaces. A pigment identical with that found in the lymph nodes is present: 1. In the hepatic cells. 2. In the endothelial cells of the capillaries. 3. In the connective-tissue cells, endothelial cells, and spaces of the wall of the portal vein. In detached endothelioid and hepatic cells, and lying free in the lumen of the portal vein. 4. In the endothelial cells lining the hepatic vein; in detached endothelial and liver cells in the lumen of the hepatic vein. No iron-free pigment is present.

Kidney. There is marked general congestion, which, however, spares the glomeruli. No hemorrhages are found. The glomeruli show no changes. The tubular epithelium is very granular, and many of the cells are disintegrating into the lumen of the tubules. Numerous pyknotic nuclei are seen. Capsule normal. Connective tissue not increased.

Tonsil. Enlarged tonsil shows general sclerosis, especially in the neighborhood of the vessels. The follicles possess wide central areas of endothelioid cells. Crypts contain degenerated epithelium and polynuclear leukocytes. The vessels are congested.

Larynx. Sections studied do not include cartilage. There is a broad superficial area of necrosis not sharply defined. The surrounding tissue is infiltrated with neutrophiles and eosinophiles, the former predominating. In the necrotic tissue are found great numbers of bacteria, those near the surface being streptococci and staphylococci, bacilli, and a long, unbranched organism, staining irregularly by Gram's method, hematoxylin, Babe's safranin, and not stained by iodin, and of various lengths, corresponding to the leptothrix maxima buccalis of Müller. In the deeper portion of this tissue only the leptothrix is found.

Lung. The triangular area resembling an infarct proved to be an area of pneumonic consolidation, with the usual characters.

The pathologic examination of the case marks it as a typical one of its kind. No new light can be thrown upon the etiology of the disease by the present study, and the main interest seems to be found in the accidents of the case, especially in the study of the hemolymph glands and the comparison of the disease under consideration with that described by Banti under the name of "splenomegaly with cirrhosis," now known as "Banti's" disease.

There is at present great difference of opinion among anatomists and pathologists as to the function or functions of the hemolymph glands, the latest contributions being from Ann Arbor, by Dr. Warthin, and from Italy, by Morandi and Sisto. The latter believe that nucleated red cells are never found in hemolymph glands, and do not admit hemoblastic functions to them under any circumstances; the glands of our case contain normoblasts in sufficient number to establish the existence of such a function, in view of the fact that the blood of the patient before death was entirely free from nucleated red corpuscles. The absence of mast cells is a noteworthy aberration from the normal.

The pathology of this case corresponds very closely with that of Banti's disease, one feature alone being absent—the cirrhosis of the liver. The sclerosis of the spleen seems to proceed much in the same manner as described by Banti under the name of "fibroadenie."

A study of the statistics of splenectomy in such cases as this makes it remarkable that this procedure is not resorted to more frequently for their treatment, this appearing to be the only certain method of cure.

The literature of the subjects considered in this report may be found as follows:

Splenic anemia: Literature collected by B. W. Sippy in *Amerrican Journal of the Medical Sciences*, vol. cxviii.

Banti's disease: Literature collected by Banti in *Ziegler's Beiträge*, vol. xxiv.

Hemolymph glands: Literature collected by Aldred Scott Warthin, in *Journal of Medical Research*, May, 1902.

Indications That Our Methods of Fumigation Are Faulty.

G. E. PFAHLER, M.D.

The problem of fumigation and disinfection is as important as it is difficult of solution. Unless disinfection is successfully done, it is only a delusion and a snare. The requirements of a disinfectant are: First. It must penetrate to every part of the room and destroy surely and quickly the most resistant forms of bacteria present. Second. It must not injure the materials with which it comes in contact. Third. It must be easy of application and not too expensive.

Rubbing the floors and walls with bread, with solutions of carbolic acid, bichlorid of mercury, or chlorinated lime; or fumigation with sulphur dioxid, chlorin, bromin or iodin gases have all had their day, and have been discarded in favor of formaldehyd gas as most nearly fulfilling the above conditions.

Judging from the results of my investigation (as well as those of others), formaldehyd will need an improved method of application or should likewise be discarded.

I have not attempted to review all the literature upon this subject, but Abbe, Rondelli, Petruschky, *Verhandlungen des Congress für innere Medicin*, 1898, and others, have found that formaldehyd gas was not a reliable disinfectant. Flügge, *Zeitschrift f. Hygiene*, 1898, vol. xxix, p. 276, found that fresh and undried sputum and diphtheritic membrane do not become penetrated; the inner side of soiled clothing, excreta in the form of scales or dried dust, the deeper parts of clothing, things in the pockets, soiled handkerchiefs, mattresses, etc., are not disinfected. He used five different methods in his experiments. First. Method of Trillat, Rouxn, Trillat, *Annals de l'Institut Pasteur*, 1896, Bon. ebenda, by which formalin in the presence of calcium chlorid is vaporized and passed into the keyhole of the room at a pressure of three atmospheres.

Second. Method of Rosenberger, *Zeitschrift f. Hyg.*, Bd. xxiv, by which tablets of formaldehyd are vaporized in the presence of 5 per cent. menthol and methyl alcohol.

Third. Sherring's method, Aronson, Diese, *Zeitschrift*, Bd. xxv, by which tablets composed of paraformaldehyd, formaldehyd, and trioxymethylen are vaporized over a spirit lamp.

Fourth. Walter Schlossman's method, by which formalin containing 10 per cent. of glycerin is vaporized and forced through the keyhole.

Fifth. Method of Flügge, by which he was enabled to vaporize 250 gm. of formaldehyd in three and one-half hours, which is about twice as much as can be obtained in any of the other methods.

Flügge, assisted by Dr. Neisser, Dr. Laschtschenke, and Dr. Polleck, found the latter method to be the most successful, but not entirely satisfactory.

They often found the staphylococcus pyogenes aureus upon the surface, and most of the pathogenic germs were found, when given slight protection in the shape of clothing, etc. Drs. William H. Park and Arthur R. Guerand, of New York, in a series of experiments in 1898, *Philadelphia Medical Journal*, September 17, 1898, found the staphylococcus pyogenes aureus and anthrax spores not killed after twenty-four hours, and other bacteria not killed after twenty-four hours when protected by one layer of cotton spreads.

Typhoid and diphtheria bacilli were not killed when placed beneath two layers of blanket. Typhoid bacilli placed at the bottom of a glass tube eighteen inches long and open at one end not killed after twenty-four hours. Bacteria placed in sealed envelopes were not killed. Bacteria in coat pockets were not killed.

By sulphur fumigation, three pounds per 1000 cubic feet, and exposed twenty hours, no pathogenic germs were killed except the diphtheria bacilli. They conclude that 60 ounces of formalin per 1000 cubic feet (ten times the amount generally used in room disinfection—6 ounces) will destroy the vitality of bacteria if the clothes are hung up so that the gas can freely circulate about and through them.

Books can be successfully disinfected when exposed in a special apparatus, not in ordinary rooms and libraries, by using 120 ounces of formalin evaporated in 1000 cubic feet of space.

Ch. Dopter, *Rev. d'hyg.*, Paris, tome xxiv, No. 2, in a recent report recommends the use of a spray consisting of commercial formalin, 40 per cent. formaldehyd, 24 c.c.; water, 976 c.c., but finds, after twenty-four hours, moulds, B. subtilis, B. mesentericus, and sometimes staphylococci.

Dr. Joseph McFarland, of Philadelphia, after a series of investigations made in 1898, *University Medical Magazine*, September, 1898, to test the value of various formaldehyd generators, concluded that more formaldehyd gas must be generated than was recommended by the manufacturers, and that this must be supplemented by cleansing and disinfecting solutions.

Dr. Daniel E. Hughes, Chief Resident Physician in the Philadelphia Hospital, and myself, have noticed epidemics of contagious diseases break out in the children's wards which had been fumigated by formaldehyd gas, to which we could trace no contagion from the outside. We often doubted the efficacy of the fumigation, but made no experiments until several months ago, when a formaldehyd candle was very highly recommended to us for disinfecting purposes. It seemed a most convenient method, but we decided to test its value before depending upon it.

In my first experiment, which I purposely made a severe test, I placed cultures of the staphylococcus pyogenes aureus near the point of generation of gas. One tube had colonies upon blood serum, open, one closed, and one just inoculated, another having a culture upon bouillon and one just inoculated, but both open. All grew well.

Considering that contagion is usually carried by the dust from the floor or upon the clothing, in my next experiment I made cultures from the surface of the floor, the bed, and the mantel, before, and repeated them after, fumigation. The cultures showed the ordinary germs found in rooms, and apparently grew as well after fumigation as before.

This experiment was repeated with a similar result. In all of these I used three times the amount recommended for 1000 cubic feet. Previous to this we had been using the Walter Schlossman method, by which formalin containing 10 per cent. of glycerin was vaporized in an apparatus which was supposed to generate enough gas in one hour to disinfect 1000 cubic feet. The tests with this apparatus were made in rooms of 700 cubic feet capacity, that were tightly sealed by means of strips of paper being pasted over all crevices. All rooms were exposed to the gas for at least twenty-four hours. Cultures in each test were made from the dust upon the surface of the floor, bed, window, and wall, before and after fumigation. In the first test the apparatus was allowed to run one hour, with the result that all cultures grew well. In the second, it ran two hours and evaporated five ounces of formalin.

All cultures grew well. A room was then exposed four and a half hours, and twelve ounces of formalin was vaporized. All cultures grew. The generator was then allowed to run for six hours, vaporized eighteen ounces and the room remained closed forty-eight hours. All cultures grew. Fifth. Gas was generated for nine hours, twenty-eight ounces formalin evaporated, and the room closed fifty-six hours. All cultures grew.

Sixth. Gas was generated for thirteen hours, thirty-two ounces formalin vaporized, and the room closed fifty hours. All cultures grew.

I then burned five pounds of sulphur in the presence of water, in the same sized room, having made the cultures as before. All grew. I then used ten pounds of sulphur in the same sized room, with the result that one culture remained sterile. This culture was made from the surface of the bed. A culture made from beneath the spread showed a luxuriant growth. The same germs in all these experiments were found after fumigation as before. They consisted of moulds, various bacilli, staphylococci and streptococci.

At the present time we do not know the specific germ causing measles, scarlet fever, mumps, whooping-cough, chicken-pox and smallpox, and as these are the diseases with which we most commonly had to deal, it seemed unimportant to isolate the various germs found in the cultures. The fact that the most common forms of bacteria were so little affected may be taken as an indication that the germs about which we are in ignorance were probably not killed. It has been our custom to scrub well the floors, walls, ceiling and furniture, and send all clothing to the laundry after fumigation.

The fact that we have been able to control epidemics depended probably more upon this latter cleansing than upon the action of formaldehyd gas.

These results indicate that the methods we depended upon locally were and are not a success. They raise doubts as to the value of attaching a fumigator to the keyhole of a large factory in which a case of smallpox has developed, and generating gas for half an hour, the windows and other openings not being at all sealed. These results also suggest that all methods and all fumigating apparatus should be regularly tested, and should answer these simple surface tests or be discarded.

All investigators seem to agree that formaldehyd gas is the best disinfectant known, but we should aim at obtaining a more satisfactory method of application which will probably mean an apparatus capable of generating the gas ten times as fast or in more concentrated form.

We should not accept the simple statement of a manufacturer of any apparatus as to its efficiency. *May* 22, 1902.

DISCUSSION.

DR. MCFARLAND thought that Dr. Pfahler's results must be correct. The speaker had examined nearly all the apparatus on the market, and not one did what the circulars claimed for it. Formaldehyd was not penetrating and did not diffuse well. Cultures on paper and muslin were more easily killed than those on materials that do not absorb moisture well. Formaldehyd did not penetrate more than two or three layers of towel or five or six sheets of paper. It was useful, however, for surface disinfection. As, however, the micro-organisms to be killed in ordinary disinfection have but little resisting power—as, for instance, those of typhoid fever and diphtheria—it was satisfactory for general use. For floors, wood furniture, etc., washing with disinfecting solutions should supplement the use of the gas.

Dr. Steele was much interested in Dr. Pfahler's studies. He did not believe there was much in disinfection by fumigation alone. The walls should be washed down with bichlorid solutions, 1 to 200 or 300. In experiments at the Presbyterian Hospital, agar plates exposed during fumigation had shown retardation of bacterial growth. He was of the opinion that Philadelphia ought to have a pay hot-air disinfecting plant. Diphtheria could not be stamped out by fumigation alone; it was necessary to make cultures from the throats of children.

A Case of Double Hydronephrosis.

L. W. STEINBACH, M.D.,

AND

DAVID RIESMAN, M.D.

Hydronephrosis has not often been the subject of discussion before this Society. In looking over the transactions we find only three instances recorded: one by A. V. Meigs,[1] in which the condition occurred in the left kidney of a woman, and was due to stone; one by F. P. Henry,[2] in a man, thirty-nine years of age, also in the left kidney; and one by Riesman,[3] in an infant, three days old. The case presented by Henry was obscure, inasmuch as no distinct cause for the hydronephrosis was found at autopsy. It was attributed to a dynamic obstruction of the ureter, due to a spastic contraction of the bladder, which was the seat of cystitis. In Riesman's case the hydronephrosis was congenital, and depended upon obliteration of the right ureter near its entrance into the bladder.

It is unnecessary to dwell upon the causes of hydronephrosis in detail, as they have been discussed in the paper published by one of us in the Proceedings of the Society.[3] They may be situated in any part of the urogenital canal, either within the canal or without, or they may depend upon alterations in the wall of the canal itself. The condition may be either congenital or acquired, but there is no special difference between these two forms except in the time of development. The greatest degrees of hydronephrosis are produced by obstruction in the course of the ureter or at its vesical opening. If the obstruction is acute and total, it is not as likely to lead to marked distention of the pelvis of the kidney as when it is slow and gradual in its development. Obstruction acting intermittently, at least in the beginning, is especially prone to produce extreme degrees of distention.

The case that we desire to report illustrates very clearly, we believe, the latter condition. The patient, Mrs. H. J. M., a widow, aged fifty-four years, having a son twenty-five years old, came under the care of one of us (S.) in 1892, stating that a short time before she had had a severe attack of pain in the right flank, and that a little while afterward she had noticed a tumor the size of an egg in that region. On examination, this tumor was found, and considered to be a floating kidney. It had gradually increased in size, but had caused no further pain until three years ago, since which time there had been severe paroxysms in both renal regions, lasting for a short time and occurring at intervals of two or three weeks. She had found relief by bathing in very hot water, and had noticed that after these attacks she voided very large amounts of urine, none being passed during the attacks. She ascribed her pain entirely to gaseous distention. The gas seemed to accumulate principally on the right side of the abdomen, in the region of the tumor. The attacks had gradually increased in severity, and had been accompanied by vomiting. They were "more severe," to quote her own words, "than having a hundred babies." The patient was extremely neurotic, and was approaching the menopause. When she was seen in consultation by one of us (R.), in May, 1900, a fluctuating tumor as large as a child's head was found in the right side of the abdomen, occupying the space between the iliac crest and the ribs above, and projecting inward a little beyond the median line. It was somewhat lobulated, decidedly cystic to the feel, and gave a distinct sensation of fluctuation. From the liver, above, it was separated by a tympanitic area, and there was a tympanitic zone, apparently the colon, running down along its inner border. The mass could be moved by bimanual palpation, and changed its position considerably when the patient turned from side to side; it also moved with respiration. In the lower part and along the right side—that is, the outer side of the mass—a small solid body, shaped somewhat like the kidney, could be discovered, from which the tumor apparently projected forward and inward. In the knee-chest position, the mass seemed to fall forward, leaving a hollow in the right loin; and here the resistance seemed to be lessened as compared with the left side. Vaginal examination revealed nothing abnormal. Urine examination was negative.

A diagnosis of hydronephrosis of the right kidney was made, and it was decided to aspirate. This was done on May 29, 1900, and about three quarts of a turbid, urinous fluid were removed. An examination of this fluid showed that it was altered urine.

The following is the result in detail: Color, slightly muddy; specific gravity, 1007; reaction, acid; albumin, 0.125 grams per liter (Esbach's albuminometer); sugar, none; urea, 0.031 per cent.; phosphates, 0.145 per cent.; chlorids, 2.21 per cent.; acidity, 0.31 per cent. expressed in sodium hydrate, 0.59 per cent. expressed in oxalic acid.

The patient was much relieved, but on the evening of the day of the operation she was seized with severe pain in the left side of the abdomen, and had suppression of urine. During the attack a mass appeared in the region of the left kidney. She was inverted, and immediately the pain and suppression were relieved, and the urine began to flow. On the following day the mass in the left renal region could scarcely be felt. A similar attack to that of May 24th occurred on June 3d and on June 6th. On each occasion the left kidney became enlarged and the urinary secretion suppressed. On June 7th a nephrotomy was done and a urinary fistula established on the left side. The patient improved, the urine flowing at times from the fistula, at times through the natural channels. She was soon able to go home, and was in fair health for some time. Eventually the urine discharged through the fistula became purulent, and a short time afterward that discharged from the bladder also became mixed with pus. The quantity diminished, and death finally ensued from uremia, seventeen months after she was first seen by us conjointly.

At the autopsy, the following notes were made:

Body of an emaciated white female, with an extraordinarily long trunk hardly at all contracted at the waist-line. Rigor mortis almost absent. There is an incised wound in the left flank, 1 x 1¼ inches in extent, from which a little gauze protrudes. In the right flank there is a slight bulging and fulness, and there are a few striæ albicantes.

On opening the abdominal cavity a large, fluctuating mass appears on the right side, representing the right kidney, and extending from an inch below the right costal border, in the nipple line, to the level of the anterior superior spine, and from the abdominal parietes on the right side inward to within an inch of the median line. Above, it is in relation with the liver, gall-bladder, and duodenum. The last is adherent to it for practically its entire extent except the upper two inches. There is a groove at the point at which the proximal portion of the duodenum joins the adherent portion at right angles. The dimensions of the cystic mass as exposed are 14 x 10 cm. Below the tumor is adherent to the transverse and ascending colon at a point corresponding with the hepatic flexure. The cecum and appendix lie in the small pelvis. The ascending colon runs up to about the umbilical line, and then makes an acute bend into the transverse colon, which descends into the pelvis in contact and parallel with the ascending colon; then the transverse colon ascends obliquely toward the region of the spleen. The appendix is 5 cm. in length and normal. The cecum is a little distended. The small intestines are of very small caliber, and are nearly all located in the true pelvis. The descending colon is contracted. and contains scybalous masses. The liver reaches to the costal border. The diaphragm extends on the right to the bottom of the fourth rib, and to the fifth rib on the left. The stomach has a nearly vertical position. The pylorus lies 7 cm. below the tip of the ensiform cartilage, and exactly in the median line. The spleen is small, and is marked by a very deep fissure; otherwise, it presents nothing abnormal. The left kidney is firmly adherent to the posterior abdominal wall and to the sheath of the psoas muscle. The adhesions at the site of operation are as tough as cartilage. The tumor on the right side is oval in shape, overlies the iliac artery, and reaches, with its lower border, to the brim of the true pelvis. On its upper surface it is crossed by a large vein running from inward and above, downward, and outward. The ascending vena cava is compressed by the mass. There are delicate adhesions between the tumor and the sheath of the psoas muscle. After leaving the pelvis the right ureter curves inward over the inner edge of the mass to its middle, where it makes a bend at right angles. The renal vessels enter the apex of the mass, being in part covered by the gall-bladder. There are no adhesions to the parietes.

After being fully exposed the mass is 20 cm. in length and 15 cm. across. It contains about a pint of clear, pale fluid. The wall is thin everywhere except on the posterior upper aspect, where several separate nodules are found, apparently representing remaining kidney structure. The suprarenal gland is present; but it is high up, under the liver, and compressed. The ovaries are rather fibroid and harder than normal; the right is larger than the left The liver is normal. The right psoas muscle is decidedly flattened by compression of the cystic kidney. The pancreas shows nothing abnormal macroscopically.

REMARKS. The right kidney, as has been indicated, is converted into a large, thin-walled sac, there being only little renal tissue left at the lower pole and outer border. The ureter, which is not dilated, runs up from the bladder and joins the sac at a considerable distance from its proximal end, running in the wall as a flattened band, which evidently has not conducted any urine for a long time. The left kidney is densely adherent at its lower half to its fibrofatty capsule, as a result of a paranephritis excited by the nephrotomy. The kidney is somewhat lobulated and enlarged.

There is a mild degree of hydronephrosis. The operative incision is about two inches long and has a healthy surface. The left ureter passes through the thick, fatty tissues of the adherent capsule, and is not enlarged. The bladder presents nothing abnormal.

The history of the case warrants us in holding that the hydronephrosis in the right kidney was due to the fact that the kidney was originally floating and that the ureter became twisted and adherent to the outside of the pelvis of the organ. In the earlier years of the woman's trouble the obstruction was probably intermittent—the open hydronephrosis or hydronephrose ouverte of Terrier and Baudouin. Eventually, however, it became closed (hydronephrose fermée), and the pressure of the fluid equalling the pressure of the secretion, the dimensions of the sac became stationary.

After tapping the patient we fully expected that she would be relieved for a time; but, to our dismay, suppression of urine set in within a few hours. The explanation for this is simple—the left kidney was also a floating kidney, but had been held in place by the intra-abdominal pressure caused by the accumulation of fluid on the right side. After tapping the pressure became exceedingly low, the kidney left its moorings and kinked the ureter. The relief obtained by prompt inversion bears this out.

The final uremia was not due to any obstruction, the kidney having been fixed by the paranephritis following the operation of nephrotomy, but to the inability of the damaged left kidney permanently to do the work of two.

There is another interesting point to be mentioned: that is, the cause of the pains from which the patient suffered, and the bloating, which was such a great annoyance to her. As the autopsy notes state, the duodenum was adherent to and compressed by the hydronephrotic sac. It is probable that from time to time this pressure upon the duodenum became extreme and caused a temporary obstruction, with consequent acute dilatation of the stomach and vomiting. In floating kidney painful attacks are quite common. They were first clearly recognized by Dietl, and are known as Dietl's crises. They are generally attributed to a twisting of the ureter or torsion of the renal vessels, but they have, no doubt, a multiplicity of causes, among them, as illustrated by our case, pressure upon the duodenum.

Regarding the hydronephrotic fluid, one point of interest is the large quantity of chlorids—2.21 per cent., as against 0.8 per cent. in normal urine. The albumin may have come from the kidney, the secretory function of which was naturally much disturbed by the increased intrapelvic pressure, but there are some authorities who hold that albumin in the fluid of hydronephrosis is the result of secretion by the mucous membrane of the pelvis and calices.

Hydronephrosis affects the right kidney more often than the left, and is more common in women than in men. Tuffier,[4] for instance, found it 21 times out of 25 in the female sex. Bilateral hydronephrosis is rarer than the unilateral; in Roberts'[5] compilation it is found 22 times in 50 cases. In our own case both kidneys were affected, but the right to a much greater extent than the left.

Our case illustrates one of the dangers of floating kidney, a condition the importance of which is greatly magnified by some writers, but also unduly minimized by others.

BIBLIOGRAPHY.—(1) Meigs, A. V. Trans. Path. Soc., Phila., 1890–91, xv, p. 173. (2) Henry, F. P. Ibid., 1887–89, xiv, 180. (3) Riesman, D. Proceedings of the Pathol. Society of Phila., n. s. vol. i, p. 253. (4) Tuffier. Annal. des malad. des organes génito-urinaries, 1874, xii, p. 14. (5) Roberts. Quoted by Senator, Die Erkrankungen der Nieren, Nothnagel's Specielle Pathologie und Therapie, 1896, p. 341.

March 13, 1902.

Acute Dilatation of the Stomach and Intestines, with Special Reference to the Condition of the Elastica.

W. M. L. COPLIN, M.D.

Dr. Coplin presented a preliminary report upon the changes in the elastica and muscular layers of the gastric and intestinal wall in acute dilatation of those organs. *May* 8, 1902.

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On Adrenalin Glycosuria and Other Forms of Glycosuria Due to the Action of Reducing Substances and Other Poisons on the Cells of the Pancreas.

C. A. HERTER, M.D.,
OF NEW YORK CITY.

[Read by invitation.]

ABSTRACT.

The starting point in this study of glycosuria is the observation that adrenalin chlorid when introduced into the peritoneal cavity of dogs is almost regularly followed by the appearance of considerable quantities of sugar in the urine.

Preparation and Chemic Characters of Adrenalin Chlorid. Of the method of preparing adrenalin chlorid little need be said here, as this subject has recently been discussed by Takamine. One point should, however, be noted. In the course of preparing adrenalin the finely disintegrated suprarenal glands are steeped in water for about five hours at a temperature varying from 50°–80° C., and later are exposed to 90°–95° C. for one hour. This temperature is sufficiently high to destroy most, if not all, diastatic ferments. The colorless aqueous solution absorbs oxygen from the air, and changes to pink and later to red or brown. The energetic reducing action of the solution is shown by its behavior to many salts. One cubic centimeter of 1 : 1000 aqueous solution of adrenalin chlorid reduced 0.042 c.c. of Fehling's solution, and 100 c.c. of the solution were thus equivalent to 0.21 grams glucose. Adrenalin chlorid reduces potassium permanganate in the cold.

There are many conditions which affect the degree and duration of adrenalin glycosuria, and some of these must be mentioned.

Mode of Administration. Subcutaneous injections of adrenalin chlorid yield only slight degrees of glycosuria.

Intravenous injections of adrenalin are followed by a larger excretion of sugar. A rise in the blood pressure is an accompaniment of the glycosuria, but the latter outlasts this rise.

Other conditions being similar, a given dose of adrenalin (from 2 to 15 c.c.) gives rise to a greater excretion of sugar when administered by the peritoneal cavity than when given intravenously. The percentage of sugar may rise to 10 per cent. or more. Sugar has in some cases been detected within fifteen minutes of the completion of the injection. The systemic blood pressure has been observed to rise after intraperitoneal injections, but not to the height noted after intravenous infusions.

By mouth, adrenalin apparently has no effect in ordinary doses.

Effect of Dilution. In the case of intraperitoneal injections of adrenalin the excretion of sugar appears to be comparatively small when a considerable degree of dilution is practised. Sometimes, indeed, glycosuria does not appear.

Size of the Dose. Within certain limits the quantity of sugar excreted appears to be proportional to the dose of adrenalin, but the relationship has not yet been carefully studied. There is reason to think that when a certain dose is followed by a very large excretion of sugar a larger dose would not have materially increased this output.

Duration of the Glycosuria. The glycosuria after a moderate intraperitoneal dose of adrenalin lasts usually somewhat less than twenty-four hours. As a rule, the glycosuria is at its height within a few hours after the administration of the adrenalin. The excretion of sugar then declines rapidly, and the urine soon contains only a fraction of 1 per cent. of reducing substances.

Total Quantity of Sugar Excreted. The total amount of sugar excreted under the conditions just mentioned is usually not more than a few grams. The very high percentage sometimes observed soon after the injection of adrenalin might lead one to expect a much larger total excretion than actually occurs. The explanation of this unexpectedly small output of sugar lies in the rapid decline of the glycosuria after the first first few hours.

Nature of the Sugar Excreted. No careful study has yet been made of the chemic constitution of the sugar excreted after adrenalin, but there is reason to think that glucose is the chief if not the sole constituent of the urine in at least most instances of adrenalin glycosuria.

Sugar Content of the Blood. Numerous observations on the sugar content of the blood before and after the production of adrenalin glycosuria indicate that in well-fed animals there is regularly an increase in the blood sugar.

Influence of the State of Nutrition. In general it may be said that the largest quantities of sugar have been observed in well-nourished dogs that had recently been fed. An adrenalin glycosuria may be obtained, however, even in dogs that have been starved for two or three days. The glycogen content of the liver is undoubtedly a factor of much importance in determining the degree of the glycosuria.

On the Apparent Tolerance Which Follows Repeated Intraperitoneal Injections of Adrenalin. Observations were made in regard to the effects of repeated injections of adrenalin in four dogs, of which only three were normal, the fourth having had the spleen and one-half the pancreas removed at previous operations.

Injections were usually made every third day with doses gradually increasing. After about one month two of the dogs died in consequence of excessive doses of adrenalin. The remaining animals, including the splenectomized dog, received injections during about two months. It was observed that the usual symptoms of an injection of average size became less pronounced than at the beginning of the experiment, and that the sugar excretion was very much less. In the case of the splenectomized dog sugar ceased to appear in the urine after the last three injections, although the doses were larger than at the beginning. The appetite was very slight at this period, and there is no doubt that the animals were in a state of partial inanition. To this state of inanition can almost certainly be attributed the failure of sugar to appear in the urine after the injection of adrenalin. This is indicated by the fact that in the case of the two dogs just mentioned large quantities of sugar appeared in the urine after small injections of adrenalin made after a two weeks' interval in which the animals took a liberal amount of food.

Why the symptoms following intraperitoneal injections should grow less pronounced with repeated doses is not yet clear. In regard to these effects a condition of actual tolerance seems to become established. It cannot be said that our experiments prove that no tolerance to the glycosuria-inducing action of adrenalin is established as the result of repeated injections. Such a tolerance is observed in the case of morphin, and apparently depends on an increased oxidizing activity on the part of the cells.

Symptoms of Intraperitoneal Injections. Within a few minutes after the injection of an ordinary dose of adrenalin the animal vomits. After twenty minutes or half an hour a period of intense excitement and restlessness usually sets in and lasts for about an hour. This condition is followed by a erpiod of prostration, which is often pronounced in small dogs. The day following the injection the appetite is usually entirely lost. On the second day the animal begins to eat again, and the signs of prostration are no longer noticeable.

After fatal doses (10 to 12 c.c. in dogs of 5 to 8 kilos) the symptoms are similar to those described, but more intense. There is repeated vomiting in many instances, and a bloody diarrhea is usual. The prostration after the period of excitement is profound, and death commonly ensues within twenty-four hours. At autopsy the intestines are found to be the seat of intense congestion or hemorrhage into the mucous and submucous layers, and the greater part of the intestinal tract may be denuded of its epithelium. The pancreas may be the seat of numerous hemorrhages and local necroses, but in other parts the normal appearances may be preserved.

Glycosuria after Local Application of Adrenalin. At an early period of the research it seemed desirable to determine whether the greater efficacy of the intraperitoneal method in the production of glycosuria was dependent on the better opportunity for the local action of the adrenalin on the pancreas. The pancreas was, therefore, exposed in a number of normal dogs, and adrenalin applied directly to the presenting surface by means of a brush. It was found that marked glycosuria follows the application of small quantities of adrenalin to the pancreas, quantities which when applied locally to other parts of the body either give rise to no excretion of sugar or to a trivial glycosuria.

As a rule, the local application of adrenalin to the pancreas leads in a few moments to a deepening in the color of the gland at the area of contact. Sometimes this local reddening of the surface of the gland is preceded by a marked pallor of the organ, but this appears to be exceptional. The glycosuria usually sets in promptly after an application of 1 c.c. of a 1 : 1000 solution of adrenalin chlorid. Usually sugar may be detected in the urine within an hour of the application. It has been observed within ten minutes of the painting. Sometimes one or two hours have elapsed before sugar was detected. The minimal dose which is capable of inducing glycosuria has not been determined, but it seems probable that in some small well-fed dogs less than 0.5 c.c. of adrenalin 1 : 1000 would suffice to cause some degree of glycosuria.

Control Experiments. It was, of course, of the first importance that control observation should be made in order to determine whether applications of adrenalin to other organs than the pancreas are not followed by glycosuria.

But other observations showed plainly that the local application of adrenalin to the pancreas is distinctly more effective in causing glycosuria than is its contact with the liver, spleen, or brain.

The pronounced nature of the glycosuria following intraperitoneal injections appears to be mainly attributable to the readiness with which the adrenalin comes into contact with the pancreas. Experimental injections of colored fluids into the peritoneal cavity give support to this view. Other experiments, which need not be described here, show that when the pancreas is rendered comparatively inaccessible to intravenous and intraperitoneal doses of adrenalin the glycosuria is less than would otherwise be expected.

Nature of the Action of Adrenalin on the Pancreas. The well-known vasoconstrictor action of adrenalin naturally suggested that the explanation of the glycosuria was to be sought in a derangement of the circulation in this gland, probably one induced by narrowing of the arteries. Two observations, however, had been made which appeared opposed to this explanation. In the first place, the local application of adrenalin is followed by an appearance of congestion and not usually by blanching. Secondly, it was found that after intravenous injections of adrenalin followed by marked glycosuria the pancreas in several instances showed on inspection no alteration in color which could be interpreted to indicate a change in the caliber of the afferent vessels. Further investigation of the subject showed very clearly that substances may be applied to the pancreas which cause marked congestion, but no glycosuria. On the other hand, it was found that a blanching of the gland, as from a 3 per cent. cocain hydrochlorate solution, was not followed by glycosuria, though there is no doubt of the vasoconstrictor action of the drug when thus applied. It was also noted that substances which, like amyl nitrite, exert a vasodilator action are capable (at least under some conditions) of inducing marked glycosuria when applied directly to the gland. It is therefore impossible to establish any definite relation between glycosuria and the vascularity of the gland or of parts of the gland. It was further observed that there is no relation between elevation of the blood pressure and the glycosuria. Adrenalin was injected into the peritoneal cavity together with sufficient nitroglycerin to keep the systemic pressure much below normal. Yet glycosuria of the usual degree was observed.

While these various experiments do not prove that vascular derangements of the pancreas are of no significance in connection with the production of adrenalin glycosuria, they nevertheless point to the conclusion that if such derangements have a part in determining the glycosuria it must be of secondary importance.

Before obtaining a clue to what we believe to be the correct explanation of the nature of adrenalin glycosuria a number of experiments were made with a view of determining whether the blood drawn from the pancreaticoduodenal vein at the height of adrenalin glycosuria contains any substance capable of inducing glycosuria when injected into the portal system of a normal animal. The observations indicate that even large quantities of blood obtained in this way cause for the most part only a slight glycosuria. As this line of investigation did not appear promising it was not carried sufficiently far to prove whether the glycosuria noted might not be dependent on the increased sugar content of the injected blood or (what seems improbable) on the presence of unchanged adrenalin in the blood.

The Action of Dilute Solutions of Potassium Cyanid on the Cells of the Pancreas.[1] We are indebted to Professor Jacques Loeb for calling our attention to the important work of Geppert[2] on poisoning by hydrocyanic acid. This suggestion was of much value for our work, as it has given us at least a clue to a better understanding not merely of adrenalin glycosuria but of other forms of glycosuria and diabetes. The fact was well known to Claude Bernard that when animals are poisoned with hydrocyanic acid the blood in the veins grows lighter in color and may assume a bright arterial hue. The explanation of this striking phenomenon has been given by Geppert in his classical work. This investigator showed that in experimental hydrocyanic poisoning the blood of the veins contains much less carbon dioxid than normal and much more oxygen, the percentage of oxygen falling only a little below that of the arterial blood. He further showed that the oxygen utilized in the organism is markedly diminished. A very careful scrutiny of all the facts elucidated by Geppert's experiments brought out the conclusion that the disturbance in the gas exchanges of the body are referable to the poisonous action of hydrocyanic acid on the cell protoplasm of the organism. This action is of such a nature that it prevents the cells from taking oxygen from the blood as in health. Hence the blood of the veins assumes an arterial tint.

With a knowledge of Geppert's work in mind it seemed very desirable to try the effects of hydrocyanic acid on the cells of the pancreas, with a view to testing the idea that local disturbances of oxidative function, limited wholly or very largely to this particular group of cells, might give rise to glycosuria. The experiments which have been made bear out the correctness of this idea.

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[1] Sodium fluorid appears to be an example of a substance which, though devoid ot reducing action, is capable of causing glycosuria.

[2] Ueber des Wessen der Blausäurevergiflung. Zeitschrift für klin. Med., 1889, Bd. xv. p. 208.

The absorption of minute doses of hydrocyanic acid by the cells of the pancreas is followed by a glycosuria of short duration.

The results of the experimentation with potassium cyanid made it important to determine the local effects of some members of that large group of substances which have an energetic reducing action. It was thought that the use of such reducing substances might interfere with oxidation within the pancreatic cells, and thus give results comparable with those obtained with potassium cyanid.

Effects of the Application of Reducing Substances to Pancreas. Only the briefest reference can here be given to the action of the various reducing substances which were employed: Sulphurous acid (SO_2); ammonium sulphid $(NH_4)_2S$; sulphuretted hydrogen; illuminating gas; carbon monoxid (CO); benzol alcohol ($C_6H_5CH_2OH$), and pyrogallol and allied phenols give rise to varying degrees of glycosuria.

Pyridin, Piperidin, and Quinolin. Experiments made with pyridin and piperidin are of a special interest because, as shown by Abel, a conium-like substance is present in the active blood-pressure-raising constituent of the suprarenal gland, and this alkaloid is known to contain a pyridin base.

In three dogs in which a 1 : 10 aqueous solution of pyridin was painted on the pancreas there followed only a slight glycosuria. Piperidin (hexahydropyridin) has a chemic constitution which indicates a much greater reducing activity than that of pyridin. In three dogs in which aqueous solutions of piperidin (1 : 10 or weaker) were brought into direct contact with the pancreas large percentages of sugar were found in the urine. It should be stated, however, that in another dog piperidin failed to cause the appearance of sugar. The explanation of these exceptional cases is not yet clear.

The Relation between Adrenalin Glycosuria and the Reducing Action of Adrenalin Chlorid. The observations to which reference has been made rendered it not improbable that the action of adrenalin in causing glycosuria is connected with its reducing activity. It was very easy to demonstrate that any oxidation of adrenalin chlorid outside the body which deprives it of its reducing power and of the characteristic Vulpian reaction with ferric chlorid also destroys its action in raising the blood pressure and in causing glycosuria. Numerous experiments with oxidizing agents, including potassium permanganate and chlorin gas, showed that adrenalin thus deprived of reducing action could be injected intraperitoneally in large amounts without producing any glycosuria or indeed any symptoms whatever. The chemic nature of the substance or substances that result from the oxidation of adrenalin chlorid is not yet .known. Violent shaking with considerable volumes of neutral oxygen for periods of one or two hours caused a reddening of the adrenalin solution, but failed to deprive it of the ferric chlorid reaction or of its ability to induce glycosuria.

Control Experiments with Substances Which do Not Reduce. These showed quite clearly that applications which are by no means indifferent in character may be made to the pancreas without causing glycosuria. Thus ferric chlorid and hydrochloric acid coagulate the protoplasm of the cells with which they come in contact, and there can be no doubt that a 5 per cent. sodium chlorid solution disturbs the normal osmotic relations. Other substances used possess a strong oxidizing action, but failed to cause he appearance of sugar.

Relation between Experimental Pancreatic Glycosuria and Interference with Normal Oxidation of Pancreatic Cells. The experiments heretofore made indicate plainly that a close relationship exists between the reducing power of a substance and the capacity of this substance to induce glycosuria when applied directly to the pancreas. There are indeed substances which possess active reducing power, but which have yielded only slight degrees of glycosuria.[1] On the other hand, there is at least one poison, hydrocyanic acid, which is capable of bringing on glycosuria, although it exerts no reducing action. As yet we have found no oxidizing agent which causes glycosuria when applied to the pancreas, but it is possible that such an agent may in time be discovered. Our present experience indicates that substances which have a strong reducing action are very much more likely to induce glycosuria than those which lack this power, although it also indicates that the ability to produce glycosuria is not always proportional to the reducing activity as measured *in vitro*. Thus a solution of adrenalin chlorid of a given reducing power will cause much more glycosuria than a solution of hydroquinon of the same reducing activity. Nevertheless, it appears that among substances of allied chemic constitution the ability to induce the appearance of sugar in the urine is at least roughly proportional to the reducing activity. We see this among substances of the pyridin and phenol groups.

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[1] Sodium : this sulphate is a powerful reducing agent, but has not yet yielded glycosuria in the course of our work.

It is not yet clear what interpretation should be put on the association of the power to reduce and the power to induce glycosuria. The striking case of hydrocyanic acid, which acts by poisoning the cell so that it no longer takes up oxygen normally, suggests that the various reducing substances act by removing oxygen from the pancreatic cells. The quantity of oxygen thus removed can be calculated. It is so small in the case of a powerful glycosuria-inducing agent like adrenalin that we must hesitate to ascribe the appearance of sugar to the mere removal of this small amount of oxygen from the cells. Moreover, we know that there are substances with marked reducing action which induce only slight glycosuria, and are acquainted with at least one poison (hydrocyanic acid) which induces glycosuria without having any reducing action. We are, therefore, inclined to attribute the glycosurias we have noted not necessarily to the reducing action of the substances concerned, but to some toxic action on the cells. This action is, however, closely connected with the power of reduction. It is possible that in some instances (as in the case of carbon monoxid poisoning) the quantity of oxygen removed from the cell is sufficient to account for the disturbance in the function of the gland.

Of the intimate nature of this functional disturbance we know nothing as yet. The instructive case of potassium cyanid suggests that in many cases the cells are poisoned in some way which interferes with their oxidative activities.

The discussion of hypotheses relating to this fundamental question will not be undertaken here.

On Glycosurias following Applications to One Portion of the Pancreas. Early in the course of the study of adrenalin glycosuria it was observed that the reddening of the gland which commonly follows immediately upon an application of adrenalin, is localized to the area of contact and superficial. This observation raised the question whether the action of the adrenalin is actually limited to the parts which show an alteration in color or whether there is a diffusion of the substance through the gland, such as must occur when an intravenous infusion of adrenalin is followed by glycosuria. In order to form an opinion on this important point a special form of experiment was devised. The pancreas was cut through at right angles at its axis, and the incision was carried through the adjoining duodenum. The bleeding vessels having been clamped or tied, an application of adrenalin chlorid was made to one portion of the pancreas, special care being taken that none of the substance should come into contact with the unpainted part of the gland. This form of experiment was used not merely with adrenalin but with potassium cyanid and pyrogallol.

The results showed, so far as the pancreas is concerned, the glycosuria which follows the local application to the portion of the gland must either depend on the absorption of the toxic substance by this portion of the gland alone or upon absorption by the unpainted as well as the painted portion. In the former case we must suppose that the substances applied to the gland do not enter the blood in sufficient amount to exert any effect upon the remaining piece of the pancreas. In the latter case we must suppose that these substances do enter the blood in an amount sufficient to act on the detached piece of the gland. If the latter view is correct, we are dealing with a phenomenon comparable to the elimination of functions that occurs when much the greater part of all of the pancreas of a dog is extirpated. But if this view is not correct, and the glycosuria arises from an effect limited to one part of the pancreas we are dealing with a phenomenon very different from the glycosuria of total extirpation. This conclusion is forced on us by the fact that a glycosuria may follow an application to much less than one-half the pancreas, whereas, as is well-known, the extirpation of one-half the pancreas from the dog is only exceptionally followed by sugar in the urine. Owing to experimental difficulties, which need not here be considered, it has not been possible to decide this important point definitely.

Control experiments, together with others that have not been mentioned, indicate that doses of potassium cyanid from four to six times as large as those required to induce glycosuria when applied to the pancreas, fail when infused into the circulation to cause the appearance of sugar. This fact renders it extremely improbable, in the case of hydrocyanic acid at least, that any of the poison painted on one portion of the severed pancreas reaches the remaining portion of the gland. If this view should prove the correct one it carries with it important physiologic corollaries which will be fully considered in another publication. The evidence at hand points to a positive specific action on the cells of pancreas and not to a mere elimination of function, as in the case of coma from pancreatic extirpation.

Relations between Human Glycosuria and the Experimental Glycosurias from the Action of Reducing Substances and Other Poisons. It is proper to refer briefly to the bearing of this research upon the interpretation of the phenomena of human glycosuria and diabetes. Our experiments show that a large variety of substances applied to the pancreas in the dog are capable of inducing glycosuria, probably by interfering in some way with the oxidations carried on by the pancreatic cells. The very intimate connection of the pancreas with these glycosurias leads one to ask whether there are not many examples of human glycosuria of similar origin. The glycosuria following conditions of asphyxia, as for instance after epileptiform seizures, can probably be referred to interference with the oxidations in the pancreas. The glycosurias noted after poisoning with carbon monoxid can, we believe, almost surely be explained by the effects of this gas on the pancreas. In the case of the ordinary chronic forms of human diabetes, with or without marked lesions in the pancreas, we are not yet in a position to speak positively, but our research suggests an explanation which may apply to many instances of this sort. It has long been known to physiologists that easily oxidizable reducing substances are constantly being produced in the organism, and that the combustion of these substances is one of the fundamental activities of living protoplasm. We know that at least one gland, the suprarenal, produces a reducing substance which is of great importance for the maintenance of the general vascular tone, and it is likely that there are other reducing substances formed by other kinds of cells, dextrose itself being for the moment left out of account. The blood containing these bodies streams through all parts of the animal mechanism, including the pancreas. If now we imagine a disturbance in the normal balance between the oxidizing activities of the pancreatic cells and the production of reducing substances in other parts of the organism, it is easy to understand how a functional inadequacy of the pancreas might arise which would interfere (through an unknown mechanism) with the normal combustion of sugar and its appearance in the urine.

If this conception be correct, the presence or absence of glycosuria in any organism may depend on the relation between two variable factors, production of reducing substances on the one hand, and oxidative pancreatic activity on the other. The effect of an excessive production of reducing substances (as from diseases of the suprarenal gland) would be equivalent to a reduction in the efficiency of the pancreatic cells. In most cases of diabetes both factors may coexist. Such a conception of the nature of diabetes helps to explain those instances in which the pancreatic lesions are slight in degree.

This idea is put out as a suggestion, not as a fact. A large amount of very careful experimental work, involving a nice technic, is necessary to determine whether it has any substantial foundation. The establishment of the fact that the blood of some diabetic patients contains an excess of reducing substances other than dextrose would give substantial support to the conception here advanced.

Histologic Alterations in the Pancreas and Experimental Pancreatic Glycosuria. Experiments indicate that histologic alterations in the pancreas are not a necessary condition of adrenalin glycosuria. Bits of pancreas removed before the production of such a glycosuria were compared with bits removed at the height of the sugar excretion. Tissues fixed in Ohlmacher's fluid and in formalin, and stained by the ordinary methods,[1] failed to show recognizable alterations.

After fatal doses of adrenalin by peritoneum, the pancreas may be the seat of focal necroses and the islands of Langerhans may be the seat of destructive changes, but we attach no significance to these lesions in their relation to glycosuria.

It is instructive to note that glycosuria may follow the application of various substances to that portion of the pancreas which contain very few of the cell clusters of Langerhans. It is impossible to state whether a more marked glycosuria follows applications to the tail of the organ (rich in islands of Langerhans) than to the head. The observations which have been made do not indicate any distinct differences in the results from painting the tail and painting the descending cephalic part, which in the dog is most free from Langerhans' islands.

The Physiologic Significance of the Experimental Method Employed in this Research. It has been shown that various substances applied directly to the pancreas are capable of acting on the cells of this gland in such a way as to induce glycosuria. Evidence has been brought out which makes it in a high degree probable that these substances, so varied in chemic composition, act through their interference with the oxidations normally carried on by the protoplasms of the pancreatic cells, though in a manner as yet unknown to us. The fact that so many substances which interfere with oxidative processes are capable of inducing glycosuria deprives adrenalin glycosuria of some of the special significance attached to it before it was discovered that so many allied varieties of pancreatic glycosuria are readily induced.

The case of adrenalin glycosuria will always be invested with that special interest which comes from circumstances that adrenalin chlorid is representative of an important internal secretion. It is, however, an essential gain to physiology that we now recognize the glycosuria from suprarenal extracts to be a particular example of glycosuria from reducing substances rather than a wholly isolated and unrelated form of disturbed carbohydrate metabolism.

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[1] Dr. E. K. Dunham and Dr. Alice C. Brown were so kind as to make these preparations.

But just as we must look upon adrenalin glycosuria as one of a large number of forms of pancreatic glycosuria from some derangement in the oxidative functions of a particular gland, so must we look upon all pancreatic glycosurias from disorders of oxidation as a particular case of disturbed oxidation. By means of local applications of substances like potassium cyanid, adrenalin, and piperidin to other types of animal cells, we may reasonably expect to interfere profoundly with the oxidations there carried on. Thus it seems likely that we possess a method which will teach us much of importance about the metabolic activities of the kidneys, the muscles, and perhaps the nervous system. Interference with the activities of the pancreatic cells gives us a striking signal, glycosuria; but there is every reason to think that other groups of cells may be thrown out of action with equal precision, if not with equally obtrusive metabolic effects. The kidney of one side can be thrown out of function, so far as oxidations are concerned, without gross mechanic insults. One would expect that while the "vital" functions are thus placed in abeyance the processes of diffusion and filtration would be little disturbed. By means of such a method it seems not unreasonable to hope for new light as to the origin of uric acid, glycuronic acid, hippuric acid, etc.

Experiments which we have made suggest that there are other substances than phlorhidzin which, acting on the cells of the kidney, lead to glycosuria. It is not impossible that adrenalin, while acting chiefly on the pancreas when intravenously infused, acts also on the kidney. On this and allied topics a further report will be made.

At present it is desired that our research be regarded as an introduction to a better knowledge of the all-important subject of oxidations and reductions in the organism, as well as a contribution to the pathology of adrenalin glycosuria.

DISCUSSION.

DR. EDSALL asked whether Dr. Herter had noted the excretion of any reducing substance besides dextrose. In one human subject to whom adrenalin had been administered, Dr. Edsall had noted the excretion of a reducing substance which did not rotate polarized light, did not ferment, did not give the reactions for glycuronic acid or pentoses, and the nature of which he had not been able to determine. It reduced Fehling's solution freely, and was for a time associated with the excretion of actual dextrose. This condition of the urine so closely resembles the conditions that have repeatedly been described as the result of the administration of nitrobenzol, and of similar substances, as to have made him more emphatically of the opinion which he had previously expressed, that the effect of adrenalin is chemic rather than due to a ferment. The substances besides dextrose commonly excreted as a result of the use of such drugs are glycuronic compounds. This substance, as noted, was not levorotatory, and did not give the orcin reaction for glycuronic acid.

Dr. Edsall had been greatly interested in Dr. Herter's suggestions concerning the wide usefulness of his method of experimentation. An earlier paper of Dr. Herter's had suggested to him the use of the same method in studying certain renal conditions, and he had begun some experimentation of this kind. The great suggestiveness of Dr. Herter's work, and the painstaking care of his attention to detail, had aroused his extreme admiration.

DR. FLEXNER congratulated Dr. Herter upon his results, which bore especially upon the theory of the production of pancreatic diabetes. The results conformed well with the ablation experiments. The application of poisons also interfered with the function, and the same result was obtained. The oxidative properties were associated with functional activity. When interfered with some results would have to follow. The method of experimentation opened a wide field for research.

DR. ESHNER expressed surprise that the local application of adrenalin produced redness. Clinically, the effect was just the opposite—blanching resulting from applications to mucous surfaces.

DR. STENGEL stated that he had been interested in the use of extracts of the suprarenal capsule, adrenalin, and other preparations, and had made use of them in clinical and experimental work for some time past. After the publication of some of the earlier physiologic papers he was impressed with the positive usefulness of suprarenal extracts in conditions in which the blood pressure was greatly lowered by weakness of the vasomotor nervous mechanism. Such a state of affairs has been shown by Krehl and others to be present in typhoid fever. The low blood pressure and dicrotism of the pulse in this condition were, according to these authors, the result of vasomotor influences rather than of weakness of the heart. Acting upon this principle, he used dried extracts of suprarenal gland and adrenalin in typhoid fever. The experiments with the dried extracts were not carried sufficiently far to afford accurate deductions. The adrenalin chlorid solution was employed intravenously in some cases of typhoidal hemorrhage when the blood pressure was so low that life was threatened and when death from collapse was imminent. Under these circumstances the addition of more or less adrenalin chlorid solution to the salt solution used for intravenous injection gave very satisfactory results in some cases. These will be referred to in a special publication later. No untoward symptoms were ever caused by the use in such injections of doses of adrenalin up to a drachm. This dose, however, if given in less dilute solutions, and quickly absorbed, as would be the case when the drug were administered in small quantities of diluting fluid, would be unsafe. In none of these cases of internal administration of suprarenal products was the urine especially examined, and the speaker did not, therefore, detect the glycosuria which has since been known to occur. Since the appearance of Blum's paper his attention has been directed toward the possibility of developing glycosuria by the internal use of the drug, and in a number of cases in which such examinations were made sugar has been found. This would, however, be referred to specially, and could be passed for the moment.

The effect on blood pressure of injections of adrenalin were marked. In one case the following figures were obtained: At 4.35 P.M. blood pressure 110 to 115 mm., 46 minims of adrenalin solution were administered; 4.45 P.M., blood pressure 165 mm.; 4.55 P.M., 160 mm.; 5.05 P.M., 145 mm.; 5.15 P.M., 135 mm.; 5.45 P.M., 125 mm. In another case, at 11.14, the blood pressure was 115 mm.; at 11.25 the injection of solution was made; at 11.35, the pressure was 135 mm.; at 11.45, 125 mm.; at 11.45, 125 mm.; at 11.55, 135 mm.; at 12.05, 150 mm.; at 12.15, 160 mm.; at 12.25, 165 mm.; at 12.35, 155 mm.; at 12.45, 140 mm.; at 1 o'clock, 120 mm.

These two cases illustrated the fugacious action of the drug as well as its promptness in a few cases. He had been able to show that repeated injections secured a degree of pressure much higher than had been present before. Thus, in one instance of surgical shock the pressure was kept high, and an operation which was at first impossible on account of the degree of shock was accomplished without difficulty from this source.

With regard to glycosuria, his experiences have been somewhat varied. In cases in which adrenalin chlorid solution were injected glucose or some reducing substance could always be detected in the urine. This appeared promptly, and generally disappeared in the course of some hours. In some cases the disappearance was complete in two or three hours; in other cases some reducing substance was still present after twelve hours. In a case of genuine diabetes the amount of sugar was considerably increased by the use of adrenalin. The speaker also examined the urine in cases in which extracts of adrenalin were given by the mouth, but in these cases was not able to demonstrate the presence of sugar.

DR. HERTER, in closing the discussion, said, in answer to a question by Dr. Croftan, that the diastatic ferment had physiologic interest, but that there was no evidence that it played a part in the production of the glycosuria. Since adrenalin and suprarenal extract acted when boiled, and since pure substances were also active in the same way, the other explanation was unnecessary. He had himself thought at first that there might be a diastatic ferment converting the glycogen into sugar, but the liver cells probably contained sufficient to do this. The reason for the disappearance of glycogen from the liver was that when the tissues had been robbed of sugar certain regulatory mechanisms were put into operation, through which glycogen was rapidly converted into sugar. The glycosuria did not occur through the excessive conversion of glycogen.

Regarding the change in color of the pancreas, he was in doubt as to how it was produced. It seemed only superficial, and, in his opinion, was not clearly due to dilatation of the bloodvessels. More likely it was dependent upon a cause similar to the reddening in cyanid poisoning, the venous blood containing less CO_2. The histologic changes might throw light upon it. He had been glad to hear Dr. Stengel's report, as it possessed a good deal of interest from many points of view. *April* 10, 1902.

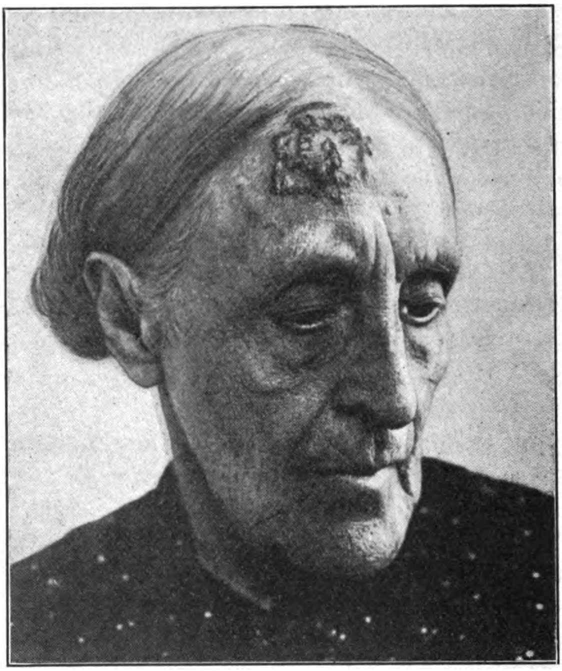
Benign Cystic Epithelioma: Report of Two Cases Presenting Unusual Features.

M. B. HARTZELL, M.D.

The two following cases of benign cystic epithelioma which I have had the opportunity to study with some detail within the past two years present clinical types of this interesting affection which, so far as I have been able to learn from a careful review of the literature of the subject, have not yet been described.

Case I.—Mrs. E. K., a woman, aged about eighty years, whom I saw through the courtesy of Dr. W. D. Robinson, her family physician, had a rounded, dollar-sized patch of nodules, made up of several smaller, coalescing groups arranged in an irregular circinate manner around scar-like areas, situated on the right side of the forehead, over the frontal eminence. These nodules, for the most part confluent, were the size of a hempseed, firm, translucent, bluish-white, with a small blue-black dot in the center of each, resembling a minute gunpowder stain. Near the center of the patch was an oblong, superficial ulcer covered with a thin crust. The patient stated that the disease had lasted six or seven years, beginning with a single lesion " like a mosquito-bite," and spreading slowly by the addition of new nodules rather than the enlargement of the old ones, which, after reaching a certain size, remained stationary. The central ulcer was of much more recent date, having appeared about two years ago. There was no pain or any other marked subjective symptom. No similar lesions were present on any other part of the body.

FIG. 1.

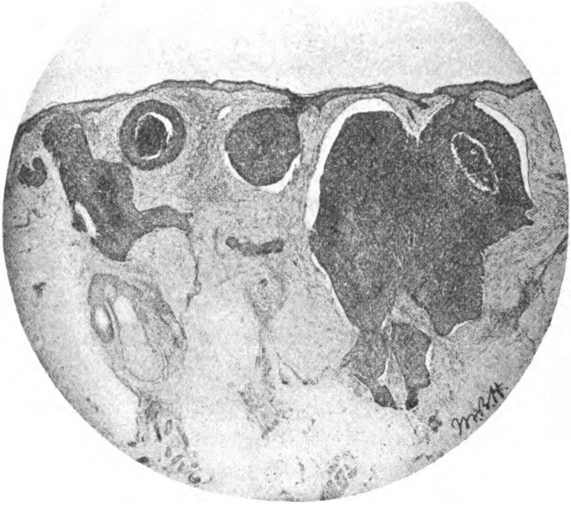


For the opportunity to study the second case clinically and microscopically, and for the use of his notes, I am indebted to Dr. Charles N. Davis, under whose care the patient had been for some time.

CASE II.—F. G., a nurse by occupation, aged thirty-eight years, in excellent general health, had six or seven dime to half-dollar-sized oval and irregularly shaped, sharply limited patches, consisting of central areas of scar-tissue and atrophied skin surrounded by a bead-like border of pinkish and yellowish large pin-head to split-pea-sized nodules, situated on the upper part of the back and chest. Three of these patches were over the right scapula, one over the left, and two beneath the left clavicle. The nodules were quite firm and slightly translucent, as if containing fluid, but none was obtained upon puncturing them. Scarring was present only in the larger patches upon the chest, where an unsuccessful attempt had been made to destroy them with the curette; but the atrophy in the remaining patches was a part of the disease process, the patient stating most positively that no treatment of any kind had been applied to the lesions upon the back. It should also be noted that in the curetted patches new nodules had made their appearance at the border of the cicatrix. The affection was not attended by subjective symptoms of any kind, and had lasted four or five years.

Lesions were excised in both cases for microscopic examination—in the first case from the border of the patch upon the forehead, and in the second from both the chest and back. The microscopic appearances corresponded very accurately with those described by previous observers, and were practically the same in both cases. The epidermis presented no abnormality except a slight thinning in places where it had been subjected to pressure from below by the cell-masses about to be described. In the upper and middle portions of the corium were numerous round, oval, and irregularly shaped masses of columnar and oval epithelial cells, the greater number of which contained a central cavity in which was a quantity of granular débris evidently resulting from degeneration of the centrally situated epithelium. (Fig. 2.) About the borders of many of these cell-masses the cells were of the columnar variety, and were arranged radially, presenting a palisade-like appearance. They stained much more deeply than the oval cells in the center of the mass, many of which took the stain feebly or not at all. A considerable number of the round and oval cell areas, when followed through a series of sections, were found to be connected with the basal columnar cell-layer of the epidermis, and had evidently taken their origin from the cells of this layer. Besides the round masses there were others presenting a great variety of irregular shapes, sending out branching processes and containing curiously tortuous cavities in their interior. Followed through a series of sections they could, in some instances, be traced to hair follicles, from which they seemed to have originated. In some of the sections made from a nodule taken from a patch upon the back of the second case a large epithelial tract presenting a reticulated arrangement was seen, resembling to some degree the structure of an angioma, but the connection of this mass with the epidermis was easily demonstrated. No such arrangement of the epithelium was observed in any of the other lesions examined. In the small epithelial masses the central cavity was correspondingly small, and was filled with an amorphous material exhibiting the staining reactions of colloid matter. In the largest cysts observed in sections of the lesion taken from the first case a considerable quantity of brown, granular pigment was noticed, but none was observed in the sections of the second case. (Fig. 3.) Around the epithelial cell-masses there was a moderate round-celled exudate, and in some instances a well-marked ring of fibrous tissue separated them from the fibrous tissue of the corium. The sebaceous and sweat glands were in appearance altogether normal.

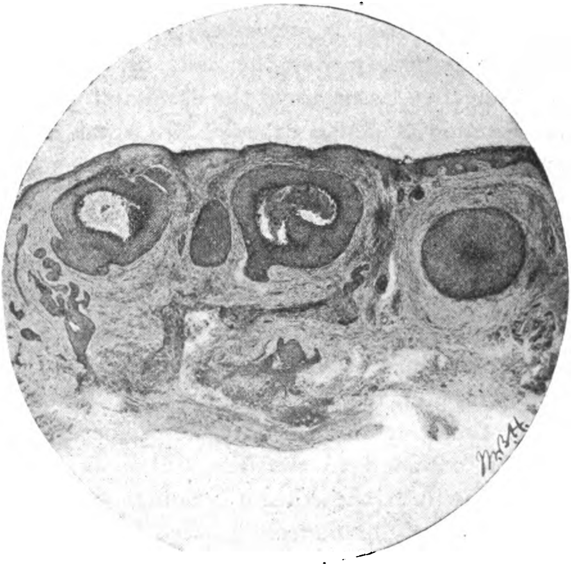
FIG. 2



From Case II.

These two cases present certain noteworthy peculiarities. In all those hitherto reported the nodular lesions were scattered about over the face and upper part of the trunk without any special arrangement; nothing like the circumscribed patches described above was observed. The advanced age, too, at which the disease first showed itself in one of the cases was decidedly unusual, as in all those previously described it first appeared early in life, commonly within the first two decades. The ulceration which occurred in this case is likewise worthy of special note, although this has been previously observed by Jarisch, White, and Hallopeau, each reporting a case in which ulceration resembling that of ordinary epithelioma took place, but the scar-like atrophy common to both cases has not hitherto been observed.

FIG. 3.



From Case I.

In 1892, under the name epithelioma adenoides cysticum, Brooke reported four cases of a cutaneous disease, all occurring in the same family—a mother and three daughters—characterized by a nodular eruption confined almost exclusively to the face, there being only a very few scattered lesions upon the shoulders and upper part of the arms. Most of the nodules contained one or more milium-like bodies, and the eruption was so abundant in places as to form lumpy patches on various parts of the face. Microscopic examination of the lesions showed that they were composed of an epithelial new-growth in the corium, which in some sections resembled a sweat gland adenoma. There were numerous epithelial tracts coiled on themselves, forming masses of various shapes in which were circular or oval cavities filled with colloid matter or horny epithelium. In other sections dense cell-masses predominated, there being few tube-like tracts. In all cases the cell-masses were separated from the surrounding connective tissue by one or more layers of palisade-like cells, which stained more deeply than the cells in the interior of the mass. The connective tissue about the epithelial masses was finer than normal, forming a dense capsule. In some of the sections the neoplastic epithelium was connected with the epidermis, and with the hair sacs, and the author believed these structures to have been the point of origin of the tumors. These cases were regarded by Brooke as being identical with the cases of Jacquet and Darier and others, which have been previously reported under various names, to which reference will again be made.

About the same time Fordyce reported two cases, occurring in a mother and daughter, resembling in all their clinical and microscopic features those decribed by Brooke. There was the same nodular eruption confined to the face and neck, and the same epithelial new-growth in the corium. Some of the tumors were made up almost entirely of densely packed epithelial cells, while in others the epithelium was arranged in bands and tracts intricately intertwined. In still others there were "pearls" and "cell-nests," as in ordinary epithelioma. In some instances the cell tracts presented an alveolar structure resembling glandular tissue. A direct connection of the cells of the new-growth with the columnar cells of the epidermis and with the external root-sheath of the hair was observed in some of the tumors, and the author thinks it evident that the epithelial masses forming the tumors were the result of the proliferations of these structures.

In 1894 Jarisch described a case of eight years' duration, occurring in a young man, aged twenty-two years, in which, besides a nodular eruption situated upon the eyelids, glabella, and temples, there were several small ulcers resembling ulcus rodens. No similar lesions were present upon any other part of the body. Microscopic examination of the nodules and ulcers revealed an epithelial deposit in the *pars papillaris* and the upper part of the *pars reticularis*. These occurred partly as round-cell masses, partly as branching cell tracts tending toward a central point which either enclosed a hair or concentrically layered, flattened, cornified cells. These cell-masses and cell tracts were separated from the adjoining connective tissue by one or more layers of darkly-stained cylindric cells. The cells within this palisade-like border varied from round or polygonal to spindle-shape, the former being found in the broad masses, the latter in the slender tracts. The connection of the cell tracts with the hair follicles could be established with ease, but no such connection with the epidermis or sweat-glands was observed. In some of the sections the cell-masses seemed to spring directly from the epidermis, but when these were followed through a series they were always found to be connected with hair follicles. Although the case was regarded by Jarisch as being identical with those described by Brooke, he gave it a new name—tricho-epithelioma, as indicating its origin from the hair follicles.

White has reported the case of a woman, aged forty-five years, with some fifty papules and tubercles upon the face, varying in size from a pin-head to a dime, and even larger, the small lesions being the color of the skin, while the larger ones were much redder. A number of the medium-sized tubercles were either depressed in the center or had begun to soften, and were covered with brown crusts. Two or three lesions were much more prominent than the rest, with abrupt, perpendicular edges and depressed centers, like Hutchinson's crateriform epithelioma. On the right upper eyelid, on the inner portion of both lids of the left eye, and on the side of the nose were open ulcers presenting the characters of rodent ulcer. Besides the lesions on the face there were a few on the neck, shoulders, and forearms, but none of these had undergone any secondary change. Bowen, who examined the tubercles microscopically, found epithelial masses in the corium, arranged in islands and elongated tracts, the latter being connected and intermingled in a complicated way. In the midst of the epithelial islands and bands were small cysts with granular or homogeneous contents; in a few, corneous material, either alone or with colloid, was present. In all the tumors connection of the epithelial mass with the lower cells of the rête could be demonstrated. No proliferation of any of the glands of the skin was found. This case is remarkable for the secondary ulceration, and the unusual size of the lesions.

Hallopeau has likewise reported a case, although under another name, in which ulceration resembling that occurring in ordinary epithelioma took place. The diagnosis apparently was entirely clinical, as no account of the histology of the lesions is given. The eruption was situated upon the lids, and had existed since infancy.

Wolters has recently reported a case which differs clinically from those previously reported, in that there was but a single lentil-sized, yellowish-red tumor over the right eyebrow. The patient was a girl, aged twenty years, and the lesion had existed since birth. It was composed of a maze of cell tracts containing large and small cysts. The epidermis was everywhere intact, but the interpapillary pegs were unequally developed and of varying shapes, and many of them were in direct connection with the cell tracts running through the cutis in all directions. The cysts contained either homogeneous colloid masses or horny, laminated globes. Besides slender epithelial tracts there were others, thicker and more massive, which seemed here and there to be connected with hair follicles, and which, like the others, contained cysts. Most of the epithelial tracts originated from the interpapillary pegs, but their origin from the hair-sheaths could also be demonstrated. The sebaceous and sweat glands, and the bloodvessels were normal.

Within a few months Pick has described a case which seems to be intermediate between benign cystic epithelioma and adenoma sebaceum, presenting some of the features of both neoplasms. A man, aged forty-three years, with a marked acne rosacea, had an eruption of small nodules seated upon the temples and forehead. There was likewise a slightly depressed, atrophied patch over the left zygoma. The nodules were found upon section to be composed of variously sized and shaped epithelial cell-masses partly anastomosing with one another. These epithelial new-formations began immediately beneath the epidermis, and extended, with their processes, down to the fat tissue. Their lobed structure recalled that of the sebaceous glands. The external border of the new-formed cell-masses was formed by cells arranged in a palisade-like manner, with well-stained nuclei. These cells were in all respects like those of the basal layer of the epidermis, with which, when the cell-masses joined the epidermis, they insensibly blended. In the cell-masses were variously sized cysts, occasionally empty, sometimes containing a mass staining intensely with acid dyes (eosin, picric acid) or finely granular material. The sweat glands showed no abnormality. The histologic picture corresponded with that presented by the cases of Brooke and Fordyce. The author concludes that the case was one of multiple adenoma of the sebaceous gland, corresponding to the sebaceous gland nevi, and that, upon the basis of such an adenoma, epithelial tumors showing the histologic peculiarities of epithelioma cysticum adenoides were formed by the proliferation of the border epithelium of the sebaceous gland acini.

In connection with this case reference should be made to the two cases of nodular eruption of the face and scalp reported by Balzer and Ménétrier, and Balzer and Grandhomme as adenoma sebaceum, since they were most probably examples of benign cystic epithelioma. Microscopically, the tumors were found to be composed of proliferating epithelial tissue arranged in lobules containing cysts, the seat of the neoplasm being the pilosebaceous apparatus.

In all the cases thus far referred to the lesions were practically confined to the face, and in all the microscope showed an epithelial new-growth having its origin in one or more of the epithelial structures of the skin.

In 1887 Jacquet and Darier described for the first time a disease of the skin characterized by an eruption of papules and tubercles confined exclusively to the anterior surface of the trunk and inner surface of the upper extremities. Darier, who examined the lesions, found that they were composed chiefly of a great number of epithelial tracts situated in the middle portion of the derma, cylindric in shape, and ramifying in all directions. Almost all of these epithelial tracts presented globular, cystic dilatations containing blocks of an amorphous, refracting substance. The arrangement of the epithelial tissue, its localization, and the multiplicity of the tumors led the authors to regard the affection as an adenoid epithelioma; and, although not able to certainly trace a connection with the sweat glands, they concluded that the neoplasm originated in these structures. As indicating the origin of the lesions, they designated the malady eruptive hydradenoma. Two years later, at the Paris meeting of the International Congress of Dermatology and Syphilis, Jacquet exhibited a second case presenting the same clinical features, but he denied the relationship of the disease to the sudoriparous apparatus, believing that the nodules were epithelial tumors developed from "erratic para-epithelial débris," and proposed a new name for it—benign cystic epithelioma. Upon the same occasion Quinquaud likewise presented a case in which there were hundreds of nodules, limited, as in the other cases, to the trunk. He expressed himself as being uncertain as to the origin of the neoplasm, but thought that it might have started from aberrant epithelial cells. At a later period Philippson reported two cases, and Torok one from Unna's clinic. The former regarded the tumors as benign epitheliomata with colloid degeneration, and endeavored to identify the affection with colloid milium; the latter considered the disease cystadenoma which had originated in the sweat glands. Jarisch and quite recently Wolters have reported cases which they considered identical with those of Jacquet and Darier, Quinquaud, Philippson, and Torok, clinically and microscopically; but they denied the epithelial character of the malady, being able, as they believed, to trace the new-formed cell-masses to the endothelium of the bloodvessels. These authors regard the affection as quite distinct from benign cystic epithelioma.

From the foregoing brief summary it is apparent that more or less confusion exists as to the exact relationship of the cases of this last group to benign cystic epithelioma and to one another.

In conclusion, it seems probable that all these cases, described under such a variety of names, represent three affections, presenting lesions which can only be distinguished from one another with the aid of the microscope, but which are quite distinct in their nature and origin: first, benign cystic epithelioma, in which the lesions are usually, but not always, situated upon the face, and have their origin in the basal layer of the epidermis and the external root-sheath of the hair; second, cystadenoma, in which the eruption occurs upon the trunk, the tumors starting in the sweat gland apparatus; and third, hemangioendothelioma, likewise situated upon the trunk, but originating in a proliferation of the endothelium of the bloodvessels.

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DISCUSSION.

DR. BABCOCK referred to a chronic and clinically benign tumor recently removed by Dr. L. W. Fox from the margin of the conjunctiva. Microscopically, this growth closely resembled those described by Dr. Hartzell—consisting apparently of epithelial invasions with small cystic cavities within collections of invading cells. This specimen was interesting in relation to the theory that these growths spring from the sebaceous or sweat glands, and indicated the correctness of Dr. Hartzell's conclusions, that growths of this type might have other sources of origin. *May* 8, 1902.

Aneurysm of the Aorta Rupturing into the Right Bronchus; Origin of the Left Vertebral Artery Directly from the Aortic Arch.

DAVID RIESMAN, M.D.

The patient, P. D., male, a native of Ireland, aged fifty-three years, was admitted to my service at the Philadelphia Hospital, on June 13, 1902, complaining of pains in the chest and shortness of breath. He had had syphilis, but no other serious illness. The pains had existed for two years, and had been principally in the shoulders. There was also a slight cough.

Examination on admission—this was the only occasion on which I saw the patient—was practically negative. The heart was weak and not hypertrophied. There were no murmurs. On the left side of the back and over the left shoulder there were marks of recent leeching, indicating that the pain had been very severe and principally unilateral. The history of syphilis, together with the continuous pain extending over two years, suggested a deep-seated aneurysm—a suspicion that was confirmed four days later by a radiographic examination made by Dr. G. E. Pfahler.

The following is Dr. Pfahler's report of the fluoroscopic examination:

"There is a large mass, five inches in diameter, occupying the region of the arch of the aorta, and extending both to the right and to the left. Pulsation is very slight."

On July 20th the patient was seized with severe pain at the angle of the left scapula, marked cyanosis, and a brassy cough. Dr. Bainbridge, the resident physician, on examination, detected a faint bruit over the middle of the manubrium. The dyspnea and cyanosis became intensified, and the patient seemed to be in imminent danger of suffocation. Under treatment he improved markedly, but on July 24th was taken with a severe hemorrhage, and died in two minutes.

The autopsy was made on the following day by Dr. Flexner, from whose careful notes I shall abstract only the paragraphs bearing upon the aneurysm. They are as follows:

The pericardium contains 100 c.c. of clear fluid. The heart is not enlarged. The vessels are prominent and the pericardium thickened. The valves are normal; the myocardium, flaccid and pale in color.

The aneurysm springs from the descending arch, and communicates with the vessel by a circular opening measuring 5½ cm. in diameter.

The sac extends posteriorly, and is intimately united with the tissues about the vertebral column; its size is about that of a fetal head at term. The sac is filled with decolorized clots. Corresponding with the aneurysm, there is an eroded area in the spinal column, involving the bodies of the fifth, sixth, and seventh cervical vertebræ and the attached portions of the ribs. The intervertebral disks are preserved from erosion. The anterior surface of the aneurysm is in contact with the right bronchus, the wall of which is eroded over an area 15 mm. in diameter. There is a communication between the sac and the bronchus, and the trachea is filled with blood.

The aorta is the seat of advanced nodular sclerosis. The arch is dilated, showing several small dilatations, corresponding with attenuated areas in the vessel wall. Opposite the main aneurysm, and somewhat anterior to it, there is a beginning aneurysm, measuring 4 by 4 mm., which can be appreciated on the adventitial surface. The heart weighs 500 grams.

The lungs are voluminous and emphysematous. In the lower lobe of the right lung are scattered hemorrhagic areas, the result of the aspiration of blood. The lower lobe of the left lung is consolidated; it is mottled, but chiefly gray in color, with numerous whitish areas, from which, as from the bronchi, pus can be squeezed.

The pathologic diagnosis was aneurysm of the descending arch of the aorta; erosion of the vertebral column and of the right bronchus; hemorrhage into the bronchus, with aspiration into the lung; multiple small dilatations of the aortic arch, with beginning aneurysm-formation; nodular arteriosclerosis; terminal pseudolobular pneumonia; congestion of the kidneys and liver; interstitial pancreatitis.

There are a few points in this case that make it interesting, although in its main features it repeats the well-known story of thoracic aneurysm. In the first place, it was clinically an aneurysm of symptoms, but not of signs.

In the second, the point of rupture, into the right bronchus, is unusual; as far as I can determine from a study of a few published statistics, the right bronchus is, of the organs in close proximity to the heart, one of those least frequently ruptured. In the collection of cases published by Oswald Browne (*Aneurysm of the Aorta*, London, 1885), of seventy-eight aneurysms of the thoracic aorta, twenty-four ruptured. In no instance, however, did the rupture occur into the right bronchus. Rupture is most frequent in aneurysms occupying the situation of the present one, as is shown by the following figures:

In thirty-one cases of aneurysm of the ascending portion of the arch, rupture took place in 5; in 29 occupying the transverse portion, rupture occurred in 7; and in 10 occupying the descending portion, rupture took place in 7. Of 8 cases of aneurysm of the descending thoracic aorta, 5 terminated by rupture. Rupture into the left pleura was most frequent (9 out of 24). Next came the right pleura and the pericardium, each in 4 instances; the esophagus, in 3; the left bronchus, in 2; the trachea, in 1; and the cellular tissues in 1.

The statistics of Crisp (*A Treatise on the Structure, Diseases, and Injuries of the Bloodvessels*, 1847; *Appendix*, 1851) show an enormous preference in favor of the pericardium as a site of rupture. In 165 aneurysms of the ascending arch of the aorta, rupture occurred into the pericardium in 41 instances; into the left pleural cavity, in 5; into the right pleural cavity, in 1; into both pleural cavities, in 1; into the esophagus, in 5; into the trachea, in 2; into the right auricle, in 3; into the right ventricle, in 2; into the left ventricle, in 1; into the pulmonary artery, in 3; into the superior vena cava, in 3; into the right lung, in 3; under the pectoral muscle, in 1; and externally, in 7.

Of 69 cases of aneurysm of the transverse arch, 3 ruptured into the pericardium, 8 into the trachea, 4 into the esophagus, 5 into the left pleura, 2 into the right pleura, 2 into the posterior mediastinum, 1 into the left bronchus, 2 into a bronchus which one is not stated), 2 into the pulmonary artery, 1 into the superior vena cava, 1 into a lung (which is not stated), and 1 externally.

Of 31 cases of aneurysm of the descending thoracic aorta, rupture occurred in 19; in 5 instances, into the esophagus; in 3, into the left bronchus; and in 2, into the left lung; 5 into the right and 4 into the left pleura.

It will be seen from these two series of statistics that the right bronchus is not mentioned in a single instance. Combining the two series, or, rather the three—two published by Crisp and one by Browne—we have a total of 343 cases of aneurysm of the thoracic aorta, with rupture in 153, or 44.5 per cent.

The incidence of rupture seems to be a little more frequent the farther away from the heart the aneurysm is situated.

In the accompanying table I have arranged the two series of Crisp and that of Browne to show the sites of rupture and their relative frequency.

TABLE SHOWING SITES OF RUPTURE OF THORACIC ANEURYSM.

	Pericardium.	Left pleura.	Esophagus.	Right pleura.	Trachea.	Externally.	Left bronchus.	Pulmonary artery.	Superior cava.	Right lung.	Left lung.	Right auricle.	Posterior mediastinum.	Bronchus (which not given).	Right ventricle.	Left ventricle.	Both pleuræ.	Under pectoral muscle.
Ascending aorta	43	5	5	4	2	7	...	3	3	3	...	3	...	...	2	1	1	1
Arch of aorta	5	7	4	2	9	1	3	2	1	...	1	...	3	2	...	...	...	....
Descending aorta	...	11	8	6	...	..	3	...	...	...	2	...	...	...	...	...	...	...
Totals	48	23	17	12	11	8	6	5	4	3	3	3	3	2	2	1	1	1

A point of anatomic interest connected with this specimen is that on examination I found four vessels instead of three arising from the arch of the aorta, the additional artery taking its origin between the left carotid and the left subclavian. It runs up to the left of the trachea, in close proximity to the esophagus; and

I take it to be the left vertebral artery, which normally springs from the left subclavian. I have looked into the frequency of this anomaly, and find it discussed by Krause, in Henle's *Handbuch der Gefässlehre des Menschen*, 1868, Bd. iii., p. 230. Krause quotes Quain, who found this anomaly five times in 291 cases. Usually when four vessels arise from the arch, instead of three, the anomaly consists in an independent origin for the right subclavian and right carotid; that is, the innominate does not exist. In my case, however, we have the innominate and left carotid, then the anomalous vessel and the left subclavian. This is the first time that this anomaly has come under my observation.

DISCUSSION.

DR. FLEXNER said that he had been interested in the presence of several partially developed aneurysms, and had removed some of the affected tissue for section. He had been able to distinguish a linear depression, suggesting rupture of the coats, probably of the elastic fibers, in the sections which had been made. Such ruptures, he thought, might be connected with the origin of aneurysms. At any rate, since the introduction of the elastic stain, ruptures of this character had been found. They might occur in health without leading to serious consequences, but in persons with angiomalacia they were more frequent and serious. Syphilis was probably one of the chief causes of such angiomalacia.

September 25, 1902.

Chronic Interstitial Pancreatitis of Syphilitic Origin.

J. D. STEELE, M.D.

The patient was a woman, aged forty-eight years. She had shown undoubted signs of syphilis for the last ten years. She had the signs of a mitral stenosis, and showed at times a trace of albumin in the urine which was of low specific gravity and of large amount. It had never at any time contained sugar in a series of examinations that extended over three years. Her last illness commenced about the 1st of July, 1901, when the liver, which had been slightly enlarged for some time, rapidly grew in size until it extended half-way between the umbilicus and costal margin. Its edge was rough and the organ was slightly tender. Some ascites developed, and there was œdema of the legs and some right-sided pleural effusion. She was slightly jaundiced, and the urine showed traces of bile. She grew steadily worse, with aggravation of the above symptom, and died about the middle of November, 1901.

The pathologic diagnosis was right-sided pleural effusion, hemorrhagic infarcts of the right lung, obliteration of the left pleura, and dilated hypertrophy of the heart affecting all four chambers; stenosis of the mitral valve and thickening of the tricuspid valve which admitted three fingers. The liver was cirrhotic, scarred, congested, and enlarged, so that it reached to the umbilicus. The pancreas was hard, and to the naked eye presented evidence of its increase in connective tissue. The spleen was enlarged and congested. The kidneys were much congested, the capsules were adherent, and the parenchyma was firm, and the consistency was normal.

The microscopic examinations of the kidney and liver showed an overgrowth of connective tissue. Sections of the pancreas showed areas in which there has been a great overgrowth of fibrous tissue, especially of an interlobar type—that is, affecting the connective tissue trabeculæ between the lobes. In most of the organs this had not been sufficient to seriously affect the glandular epithelium, and was more marked around several of the lobes, which were so pressed upon as to produce almost total atrophy of the secretory cells. The overgrowth and fibrous tissue were so marked that it became intralobular as well as interlobar.

The islands of Langerhans are not at all affected, either in number or in the amount of connective tissue within these bodies. Thus, even in the most sclerotic portions the islands resisted the action of the fibrous tissue, and were unaltered.

September 25, 1902.

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